

Dietary Inflammatory Index and chronic pain in an adult, non-institutionalized civilian population of the US

by

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ABSTRACT

Chronic pain (CP) has a high prevalence worldwide. Yet, the mechanisms behind it are largely to be explained. One possible cause of CP is inflammation. The Dietary Inflammatory Index (DII) assesses the tendency of diet to cause inflammation.

The association between DII and presence of chronic pain in neck and/or lower back was studied, as well as pain duration longer than 24 hours and longer than 3 months. The hypothesis was that higher levels of DII are associated with increased pain presence and duration. A population of 3966 individual taken from the 2003-2004 NHANES survey was considered. Baseline characteristics were analyzed with chi-square test and t-test. Univariate and multivariable analysis were performed using logistic regressions. Manual selection method was used for final model construction. The analyses performed were cross sectional.

DII levels were deemed significantly associated with presence of pain in lower back and/or neck in the final model ($p= 0.0346$; Odds Ratio (OR)= 1.031; 95% Confidence Interval (CI)= 1.002 - 1.060) which included another four relevant covariates. DII levels were also deemed significant in association with pain longer than 24 hours ($p<.0001$). Lastly, DII levels were significantly associated with pain lasting longer than 3 months in the univariate analysis ($p= 0.0164$; OR=1.012 95%CI=1.042 - 1.124), although this association was lost in the multivariable analysis ($p= 0.2956$). From the results of this study, it appears that higher levels of DII (as a result of a pro-inflammatory diet) may play a role in the etiology mechanism of chronic pain and possibly in its perpetration.

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ABBREVIATIONS

CNS	Central Nervous System
CDC	Center for Disease Control
CP	Chronic Pain
CLBP	Chronic Low Back Pain
CRP	C-Reactive Protein
DII	Dietary Inflammatory Index
DP	Dietary Pattern
FFQ	Food Frequency Questionnaire
IASP	International Association for the Study of Pain
NHANES	National Health And Nutrition Examination Survey
PAG	Periaqueductal Gray
PSF	Psychosocial Factors
PDP	Prudent Dietary Pattern
WDP	Western Dietary Pattern

CHAPTER 1: INTRODUCTION

1.1 Background

1.1.1 Chronic pain and inflammation

Chronic pain is a common morbidity affecting approximately 20% of the adult population in Canada ^[1]. Chronic pain has a high impact in terms of cost in Western countries^[2]. In the United States, around 30% of the population have a chronic pain condition, bringing the total annual cost to 500–600 billion dollars ^[3, 4]. In Canada, a study by Phillips and Schopflocher reported the costs related to chronic pain to be higher than HIV, cancer and heart disease combined ^[5]. This figure takes into account direct health care costs (more than \$6 billion per year) and estimates of productivity loss including sick leaves (\$37 billion per year). Moreover, a recent study on incremental costs in the province of Ontario found that the average cost of treating chronic pain patients is ~51% higher than patients without chronic pain ^[6]. In countries of the European Union, literature in the area of chronic pain is scarce ^[7]. According to a study by Tudler et al. the overall cost of low back pain (both acute and chronic) is 1.7% of the entire gross domestic product ^[8] in the Netherlands; 20% - 30% of this figure is due to chronic low back pain alone. In general, most studies have been focusing on chronic low back pain, as it is the most prevalent chronic pain in the general population ^[9].

The burden of chronic pain is not limited to quantifiable monetary expenses; disability and quality of life are negatively impacted as well. Chronic pain

has been described as a contributing factor for developing disability ^[10], and is considered one of the leading causes for disability worldwide ^[11]. Moreover, longer durations of pain are correlated with worse disability outcomes ^[12]. Disability has also been found to be a negative predicting factor for patients' outcomes ^[13], and to particularly affect and reduce work productivity ^[14], and to negatively impact quality of life ^[15]. The mechanisms behind these associations seem to be mediated by psychosocial factors ^[15] and work satisfaction ^[16].

The causes and mechanisms behind chronic pain are still largely unclear ^[17]; multiple factors are described in the literature as being involved in the origin and perpetration of chronic pain ^[18]. These factors include some general, non-organic aspects (e.g., psychosocial factors ^[19]) as well as various organic aspects (e.g. neuro-modulated sensitization ^[20] and health status ^[15] among others). These factors are covered in detail in the literature review chapter.

Of particular interest to this thesis is the literature finding of an association between inflammation and chronic pain. For example, chronic pain manifests clinically as different subtypes, including single site (or regional) chronic pain and multisite chronic pain ^[21], which present dramatic differences in prognosis. Multisite chronic pain is more likely to be associated with poorer functional outcomes ^[22], disability ^[23, 24] and risk of developing depressive and anxiety disorders ^[25]. In 2014, one study reported that these patients had higher levels of inflammatory markers and an increased immune response compared to single-site pain patients ^[21].

Similar results were reported by another study in 2015, which showed a significant association between concentration of substance P (an important inflammatory marker) and level of pain in patients with a systemic inflammatory

disease (Rheumatoid Arthritis) whereas the association was not observed in patients with Osteoarthritis (a degenerative disease characterized by the absence of systemic inflammation) ^[26]. Just like substance P, many other factors correlated with inflammation appear to be contributing to the origin or perpetuation of chronic pain in the human body (see literature review section of this manuscript). These findings suggest that patients with higher pain levels tended towards an overall higher inflammatory status ^[27], which highlights a possible relationship between the inflammatory status of the patient and the presence, quantity, and quality of pain.

A variety of biomarkers that are involved in the inflammatory process have also been associated with specific diets; these pro-inflammatory diets seem to increase the human body's inflammation level ^[28, 29]. Inflammatory biomarkers involved with diets are discussed in the literature review chapter of this thesis. Even though these findings suggest a possible link between diet, inflammation, and chronic pain, there is a literature gap on the interaction between diet and chronic pain.

1.1.2 Dietary Inflammatory Index

Specific diets have been found to have a different inflammatory impact on the body ^[28, 30-36]. Each food has different properties regarding the inflammatory response elicited in the body ^[37], where quantity and frequency of each food's consumption play an important role in the overall inflammatory effect ^[38-43]. For this study, it was paramount to quantify the impact that a specific diet as a whole had on each individual involved. For this reason, the Dietary Inflammatory Index (DII) has been used to test the relationship between the presence of chronic pain and diet-related inflammation level.

The DII is a widely used measure for assessing the inflammation level related to a specific diet; its latest and most updated version (2010), described by Shivappa et al. ^[44], was used for this study. The DII aims to quantify the amount of inflammation due to specific combinations of food intake. It was developed using worldwide data on diet and inflammation, and has been validated ^[30, 45]. In the creation of the DII, each specific food was assigned a value according to its effect (pro- or anti- inflammatory) on the human body. This food-specific value was then factored in with quantity and frequency of consumption in an individual's diet to calculate the final overall DII score. The dietary data was available at the CDC (Center for Disease Control), and it was part of the National Health And Nutrition Examination Survey (NHANES). The NHANES is an ongoing program of surveying the American population to assess health status and nutritional habits. Within this survey, the dietary data were collected using the Food Frequency Questionnaire (FFQ), a semi-quantitative questionnaire adapted for the US population. The complete process on how the DII was developed, as well as how it is calculated, is described in chapter 3 of this manuscript.

1.2 Rationale

There is a high degree of controversy regarding the understanding of chronic pain's underlying etiological mechanisms, treatment policies and protocols. When considering the prevalence, impact (both on society and individuals) and high amount of resources allocated to its treatment, clinical results are still far from satisfactory ^[46].

Chronic pain sufferers account for a significant portion of the patients seen in outpatients physiotherapy clinics (up to 20% of total population and up to 80% of total revenue) ^[47]. This statistic clearly points to the need of these patients to frequently and regularly visit outpatient clinics, which highlights the lack of long-term results provided by physiotherapy treatment. Outside of physiotherapy settings, chronic pain is often managed by physicians with drugs ^[48], an approach that leads to other serious side effects ^[49, 50], and in most cases, fails to provide a valid long-term solution ^[51].

Chronic pain in the neck and in the lower back were chosen for this study due to their relevance for the general population ^[52], since they are a most common source of disability ^[53, 54] and their high prevalence is expected to increase in the next few decades ^[9].

A major issue for a clinical approach to chronic pain is that the etiology behind chronicity is still largely unclear. Overall, chronic pain has been associated with multiple factors ^[55] (which are all described in the literature review chapter of this thesis) and should be approached accordingly ^[56]. No relevant research on the association between diet-related inflammation and chronic pain could be found in literature. The present study contributes to the further understanding of the mechanisms linked to chronic pain.

Since inflammation impacts the experience of pain, diet-related chronic inflammation may also affect the overall experience of pain (presence, severity, number of pain sites, and duration). The underlying mechanism could be that specific dietary patterns elevate, even slightly, the level of systemic inflammation in the body, counteracting or hindering the body's attempt to recover from acute pain. Therefore,

people with certain dietary patterns defined as pro-inflammatory would be more prone to increased, persistent, or chronic pain; their bodies are less able to recover from a painful state due to the heightened systemic inflammation ^[57].

Current evidence indirectly supports the association between DII scores and chronic pain by describing possible mediating pathways. For example, higher DII scores have been associated with higher levels of inflammatory markers, such as C-Reactive Protein (CRP) ^[30], substance P ^[58], interleukin 6 (IL-6) ^[34], and homocysteine levels ^[59]. Different studies show that heightened levels of these markers are associated with higher incidence of certain inflammation-based conditions, such as colorectal cancer ^[60], asthma and decreased lung function ^[34], obesity ^[61], prostate cancer ^[59], lower bone mineral density ^[32], and, most importantly for this study, chronic pain ^[58].

Another possible mediating mechanism between diet and inflammation can involve the gut microbiota. It has been shown that dietary patterns influence the state of inflammation of the intestines by affecting the gut microbiota ^[62, 63] and by creating a local immune inflammatory-type response ^[64, 65]. This local inflammatory-type response can become chronic and systemic ^[66] and cause a multi-systemic sensitizing effect, which in turn can cause acute pain to become chronic. Another possible mechanism involving the gut microbiota involves the reciprocal modulation of the brain and the gut microbiota; this modulation is mediated by different signaling mechanisms (both neurotransmitters and endocrine hormones), and has been linked to the pathophysiology of a wide array of conditions involving the human brain, including chronic pain ^[67]. More research is needed in this area.

1.3 Purpose of this study

The goal of this study is to investigate the association between diet-related inflammation measured with the DII and chronic pain. This was achieved by analyzing the 2003-2004 US National Health and Nutritional Examination Survey (NHANES) data ^[68].

A secondary objective was to determine if individuals with higher DII are more likely to experience pain for a period of time greater than 24 hours. This objective addresses the time-dependent aspect in the determination of pain as chronic (pain lasting more than 3 months). For the complete definition of chronic pain refer to the review section of this manuscript. In 2006, the CDC used this cut-point (people who experience pain for a period >24hrs) in an assessment of the general population of the US affected by chronic pain ^[69]. This was later found to provide a conservative estimate ^[70] in the chronic pain assessment and was therefore considered relevant for a good estimation of chronic pain prevalence in the US population ^[71].

A tertiary objective was to study the length that patients that had pain for, among those who responded positively on having pain for longer than 24 hours in the previous month. This variable has been assessed as a dichotomous variable using a cut-off point of three months. The objective was therefore to assess if higher levels of DII were associated with pain experienced for longer than 3 months. As mentioned earlier in this chapter, this timeline has been used to define chronic pain in literature and clinical practice.

1.4 Organization of this study

This thesis consists of five chapters. Chapter 1 is a general introduction to the study. Chapter 2 covers the relevant literature review regarding chronic pain, inflammation (with a particular focus on diet-related inflammation), and the DII. Chapter 3 focuses on the methods utilized for this research, including information on data collection, study sample (inclusion and exclusion criteria), calculation of the DII, treatment of relevant covariates and statistical methods used. Chapter 4 presents an analysis of the results obtained from the methods described in chapter 3. Chapter 5 offers a discussion of the significance and limitations of the results, highlighting the conclusions that can be drawn from this analysis. An appendix section can be found at the end of this manuscript with the relevant parts of the questionnaire used to collect the data used in this study.

Due to the manuscript format utilized in this thesis, some repetitions can be found throughout.

CHAPTER 2: LITERATURE REVIEW

2.1 Epidemiology of chronic pain

The International Association for the Study of Pain (IASP) defines chronic pain (CP) as pain that persists beyond the average healing time for the involved tissues ^[72]. The usual timeframe that is pragmatically accepted and used is a period of 12 weeks (or 3 months) after which acute pain is defined as chronic.

When analyzing CP prevalence, some authors estimate that approximately 19% of the adult population in Canada is affected ^[73], suggesting that CP is more prevalent than diabetes ^[74] or asthma ^[75]. In the US, the prevalence ranges between 20% ^[76] and 30% ^[77], while in Europe it was found to be around 20% ^[78]. Part of the issue with CP is that, in spite of the condition's high prevalence, only 2% of people affected by CP will seek help at a specialized clinic ^[78]. The other 98% will manage their condition through their primary physician, mainly by pharmacological intervention ^[79], despite evidence that the pharmacological intervention still lacks in providing significant, reliable, and consistent improvement ^[80].

The financial burden of CP is considerable, adding up to over CAD43 billion/year in Canada ^[81], €200 billion/year in Europe, and \$635 billion/year in the USA (based on 2008 data)^[3]. This burden comes from both losses in productivity and active treatment costs. When taking into account the high impact that CP has on both the affected individuals and on the entire society, the understanding of the underlying

etiological mechanisms, treatment policies and protocols, as well as clinical results are still far from satisfactory ^[46].

CP is a complex condition that involves many factors, including both organic and non-organic aspects. Non-organic aspects involve multiple dimensions intertwined into the large umbrella known as psychosocial factors, while examples of organic factors include acute uncontrolled pain, age, gender, physical deconditioning and genetic factors. From a general perspective, more research is needed to further understand CP and its mechanisms.

2.1.1 Non-organic contributing factors.

Psychosocial factors (PSFs) are a broad variety of factors that have been associated with the overall experience of CP ^[19, 82, 83]. Even though the mechanisms behind this association are still unclear ^[84], its existence and relevance is known and commonly accepted in pain medicine ^[19, 82]. The various factors involved in the psychological process of chronic pain are interconnected and should always be considered as part of a whole, unique process. PSFs that impact CP can be categorized into two distinct classes for analysis purpose: psychological aspects (treated in section 2.1.1.1) and social aspects (discussed in the section 2.1.1.2).

2.1.1.1 Psychological Factors.

From a general standpoint, psychosocial factors have been associated with many conditions ^[85] (e.g. heart disease ^[86]), as well as with the general health

condition of individuals ^[87]. Factors like depression, catastrophizing, uncontrolled stress and hostility have been widely described in literature as having an overall impact not only on individuals but also on public health ^[87].

A variety of PSFs have also been associated with CP, with the relevant ones listed below.

2.1.1.1.1 Attention.

The ability to direct and focus one's attention has a strong connection with pain ^[88, 89]. On one hand, it is a key functional goal of pain to heighten the attention level and to direct this attention towards protecting from a threat, which is usually a possible cause of injury for the human body ^[90]. This understanding helps explain why it is difficult to ignore pain, even when present under conditions that are not necessarily of immediate threat, like chronic pain. On the other hand, attention is a component of the pain experience, since hypervigilance (excessive attention towards pain) has been associated with presence of chronic pain ^[91].

Some studies suggest that attention becomes impaired in patients with chronic pain, and the inclusion of attention training exercises in those patients' treatment may improve the clinical outcome ^[92, 93]. These findings point out a possibility of a reciprocal interconnection between pain and attention: pain appears to impair one's ability to focus the attention to perform meaningful tasks, yet attention seems to be needed in order to break the pattern of chronicity. ^[94]

2.1.1.1.2 Interpretation of noxious stimulus.

A noxious stimulus is a sensory response to a potential or actual damage to body tissues ^[95]. It may cause pain, but the link may involve other factors as well ^[96]; pain is not always elicited at the occurrence of a noxious stimulus.

Interpretation of the noxious stimulus includes a range of different factors that are deeply interconnected with the emotional status of the individual ^[97]. The interpretation depends upon previous experiences that the patient had, which impacts how the patient's brain processes current experiences. A good example for this mechanism is allodynia, defined as a noxious stimulus that would not normally be experienced as painful.

Emotions seem to play an important role in the processing of pain in some predisposed patients ^[98]. Patients with different personal stories (e.g., previous trauma) and interpretation patterns (e.g., anxiety ^[99, 100]) may process the experience of pain in completely different ways. Thus, the interpretation of pain is dependent on beliefs and attitudes ^[101, 102], expectations ^[101, 103], cognitive sets ^[84] (e.g., pain catastrophizing ^[104]), emotion regulation ^[105] (e.g., depression ^[100]) and coping strategies ^[97].

2.1.1.1.3 Pain Behaviors

Certain behavioral approaches to pain have been shown to negatively affect the overcoming of chronic pain patterns ^[106]. In the literature, there are three main behavioral models highlighted that negatively affect chronic pain: fear-avoidance, misdirected problem-solving and diathesis-stress.

The fear-avoidance model provides a possible explanation on how acute pain transitions to chronic. This model is based on the idea that the fear of pain or re-injury can cause an increase in disability to a greater extent than the pain itself. The increase in disability is due to decrease in activity participation which is justified by fear of re-injury or further damaging ^[107]. The reduced amount of activity participation creates a spiraling pattern where the individual becomes progressively less engaged in activities of daily living, which then results in physical deconditioning or emotional withdrawal due to social implications. Both of these scenarios can contribute to the increase in sensitivity to pain ^[107, 108].

The misdirected problem-solving model is based on an inappropriate application of the otherwise useful problem-solving approach that is characteristic of the human species ^[109]. In the case of chronic pain, the tendency to focus on problems in order to solve them results in a *hypervigilant status*, which fragments attention, fueling worries and fears and creating a perseverance loop (“vicious cycle”) that prevents patients from resolving pain ^[110].

The diathesis-stress model is based on the idea that a baseline amount of stress in an individual who experiences pain would reduce the ability of such an individual to deal with the recovery process, thus predisposing them to chronic pain ^[111]. This model puts a great importance on the role of emotional processing and highlights the higher risk that emotional distress yields in regards to CP ^[112].

2.1.1.2 Social factors

The “social” component of PSFs includes all sociodemographic aspects that have been linked to CP; the common denominator of these aspects can be summarized by the word deprivation.

Deprivation in certain social aspects seems to be associated with the presence of chronic pain. There are three main areas of deprivation that are related to the presence of chronic pain: low household income ^[113], belonging to deprived socio-demographic groups ^[114] and a lower level of education ^[114, 115]. In relation to these areas, employment status plays a key role as well ^[116].

Social factors are therefore relevant, and yet they could be better addressed through politics rather than in clinician’s practice, as some authors suggest ^[114, 117]. It is nonetheless important to acknowledge the presence of these factors and keep them into account when studying CP.

2.1.2 Organic contributing factors.

There are many organic factors that play a role in patients’ chronic pain experiences. For analysis purposes these factors can be divided into two categories: organic factors that cannot be modified (section 2.1.2.1) and those that can (section 2.1.2.2).

2.1.2.1 Non-modifiable factors.

2.1.2.1.1 Sex

Recent studies suggest very strong evidence on the higher prevalence of chronic pain in females ^[118-121], even though the reason behind it is not clear ^[118, 119].

Women show higher prevalence of a variety of different chronic conditions including chronic pain ^[122]. The majority of these conditions are currently considered to be mediated by an heightened inflammatory state ^[122]. One study points out that the inflammatory process could be involved ^[123]. This higher prevalence could be mediated by organic, structural differences in specific inflammatory pathways which may favor inflammation ^[123] and pain sensitivity in women ^[122].

In contrast a few other studies point out (although with a weak evidence level) that part of the mechanism for chronic pain in women could be mediated by the hormonal menstruation cycle ^[124]. These hormones have an anti-inflammatory effect ^[125], which appears contradictory to the above-mentioned inflammatory-based theory.

A survey of the current literature shows that there is not enough evidence to support either theory. Nevertheless, it is important to recognize the difference between sex and take it into account when analyzing data involving pain.

2.1.2.1.2 Age

An association between age and CP has been shown, yet there is still uncertainty on the effect of aging in older people, as it relates to CP. While all studies show a linear positive association between CP and increasing age up to the age of 65, there are differences when it comes to older age. Some studies show that the prevalence of CP in older populations keeps increasing, virtually following the linear

progression evidenced in younger people and middle age ^[126]. Other studies found that the overall prevalence of CP decreases in older populations, creating the peak of CP prevalence in the age group between 45 and 65 ^[127].

The reason for these different findings is not clear, as it could have different reasons. It could be either a mere survival effect (people without CP have longer life expectancy), or an artifact (older people not reporting CP because they consider it non-relevant or normal for their age), or it could have in fact a protective effect.

2.1.2.1.3 Genetics

Genetics play a role in the incidence of CP ^[128, 129], though evidence is not strong, mostly due to the limited number of studies in the area. All of the studies available seem to point in the same direction: a complex picture of chronic pain conditions (including fibromyalgia ^[130]) is mediated by minor contributions from a high number of polymorphisms involving single nucleotides (single base mutations). Each of these nucleotide is involved with a different functional pathway, and each has a different impact on the condition mechanisms ^[128, 131, 132].

While the genetics of an individual clearly cannot be changed or addressed directly, the expression of genes within the human body can be influenced through a process known as DNA methylation. This process, being a modifiable factor involved in CP, is described later in the current chapter.

2.1.2.1.4 History of trauma, injury, interpersonal violence

Two large studies ^[133, 134] found that a self-reported history of violence or abuse perpetrated either at home or in a public place was associated with an increased risk of having CP later in life. The reasons behind this have not been established yet.

2.1.2.2 Modifiable factors (non-pharmacological)

2.1.2.2.1 Presence of pain

Presence of acute, uncontrolled pain ^[135] and presence of chronic pain in another body site ^[136] are strong predictors of CP. This association follows a positive linear trend: higher pain scores, longer durations of experiencing pain, and more places involved with pain in the body are all associated with higher chances of developing CP ^[137, 138]. This emphasizes that health care professionals have to recognize, acknowledge and address any reported pain from the patient in a timely manner. Failing to do so could put the patient at higher risk of developing CP.

CP affects the brain through the remodeling process of neuroplasticity ^[139]; changes in the brain happen very early on in painful stages (as early as 8 days) ^[140], and early intervention can help address the problem before the changes become chronic and harder to address ^[141].

2.1.2.2.2 General Health

2.1.2.2.2.1 Co-morbidities

The prevalence of CP is higher in individuals who are affected by other chronic conditions when compared to people who are not ^[142]. There is evidence in the literature for a number of these conditions, including heart diseases and

respiratory diseases ^[143]. The reason is not clear, but it may be a consequence of the disabilities associated with these conditions ^[144]. Additionally, it may be caused by an increase in pain sensitivity in the periphery, which can then trigger chronic pain-like neuro-patho-physiological adaptation, both in the central and the peripheral nervous system ^[145].

2.1.2.2.2.2 Sleep

A number of studies point out that sleep disturbances are a predisposing factor for chronic pain. These results highlight the role of sleep quality as a predictor of pain onset and persistence ^[146] as well as pain intensity ^[147].

The mediating mechanisms for this causal relationship are still to be elucidated ^[148].

2.1.2.2.2.3 Obesity

Obesity has been associated with chronic pain ^[149]. The causal relationship may be mediated, at least in part, by the increased weight bearing demand often paired with poor physical activity ^[150]. This combination has been pointed out to negatively affect joint and soft tissue extensibility ^[151].

As different studies suggest, there are other factors linking CP and obesity: familiarity and environmental factors have been found to play a major role ^[152-154]. Overall obesity needs to be taken into account when studying and treating CP (at least as a secondary or tertiary intervention).

2.1.2.2.2.4 Physical activity

There is limited evidence that physical activity benefits CP. Likely, the lack of research with broader generalizability regarding chronic pain conditions and populations is the main reason for this limitation ^[144]. A few studies which used different protocols of Yoga, Pilates and Tai-Chi obtained modest results and their generalizability is very limited ^[155]. Thus, the most effective exercise protocols that could be found in literature have been those specific to each patient's situation, rather than a generalized protocol for all CP patients ^[156].

More research is needed in this area to clarify which clinical sub-groups of patients would benefit the most from specific types of interventions.

2.1.2.2.2.5 Alcohol consumption

Alcohol has an analgesic effect that is limited in time, and yet it is still widely used as a self-medication ^[157]. The major issue with alcohol use as an analgesic is that, paired with limited efficacy, it also creates tolerance, which may lead to alcohol abuse. Withdrawal from alcohol generally increases pain sensitivity, which makes the withdrawing process harder and can lead back to alcohol or other substances abuse in order to cope with the increased pain ^[158].

A recent study pointed out that CP patients are less likely to turn to alcohol, when compared to the general population ^[159].

2.1.2.2.2.6 Smoking

Current literature shows evidence of an association between smoking and both increased pain as well as a higher number of pain sites ^[160-162]. Some authors

suggest that the negative effects that smoking has on the human body yields a negative impact on CP as well ^[163], however no causal relationship has been demonstrated.

Another aspect of the relationship between smoking and CP that is yet to be clarified is whether smoking cessation has a positive effect in reducing CP. The compounded fact that smoking cessation is usually lower in CP patient makes this study even harder to be completed ^[164].

2.1.3 Neurological modulation of CP

There are multiple neurophysiological changes that occur in the human body when acute pain transitions to chronic. The causes and mechanisms behind the process are not entirely clear, but according to current understanding, there are at least two neurological processes involved, sensitization and modulation, each of which is then divided into two parts. These processes happen simultaneously, influencing each other along the transition between acute to chronic pain.

2.1.3.1 Sensitization

2.1.3.1.1 Peripheral

Peripheral nociceptors respond to noxious stimuli when the critical intensity threshold is reached. As a consequence, conduction, transduction and pain threshold of the afferent fibers are enhanced, facilitating the likelihood of spontaneous firing ^[165].

Following this initial stage, the peripheral nervous system goes through a phase of inflammation (known as neurogenic inflammation), where a cascade of inflammatory markers is initiated in the involved nerve area. Physiological consequences of the neurogenic inflammation are an increase in the number of channels and receptors on the cell membrane, an increase in ion channels permeability and the expression of genes facilitating pain transmission ^[166].

The combination of these events contributing to the local peripheral nerves excitability is known as “peripheral sensitization”. This stage typically lasts a few days to a few weeks depending on the severity of the initial stimulus, though in some individuals the recovery process from a state of nociceptive alertness does not resolve. The reasons behind this failure to recover are not clear, but recent studies point out the possible involvement of factors including systemic immune/inflammatory heightened response ^[167], genetic factors ^[131, 132], and environmental involvements ^[168].

2.1.3.1.2 Central

A prolonged state of peripheral excitability may lead to an “overflow” of excitability in the central afferent structures of the nervous system, from the spinal dorsal horns to the centers for pain in the brain ^[169].

Specific areas of the brain have been found to have an activity level altered by pain presence: the primary somatosensory cortex (S1), the secondary somatosensory cortex (S2), the prefrontal cortex (PFC), the anterior cingulate cortex (ACC), the cerebellum, the thalamus, the amygdala, the insula, and the mesolimbic reward circuit ^[170-172]. These areas are not solely dedicated to processing the

experience of pain, which again highlights how multi-layered the processing of that experience is for humans ^[173].

A variety of chemokines, cytokines, and neuropeptides are involved in this multi-faceted process that constitutes the pathophysiological state of central sensitization ^[174]. In this state, the amount of stimuli necessary to reach the threshold for pain becomes significantly reduced. The neurophysiological process involved in central sensitization as a consequence of enhanced central activation of nociceptive pathways is mediated by a group of mechanisms known as N-methyl-D-aspartate (NMDA)-dependent mechanisms ^[175]. An example of chronic pain condition where the NMDA-dependent mechanism plays a key role is the phantom limb pain ^[176, 177].

2.1.3.2 Modulation

2.1.3.2.1 Descending

Descending modulation has been found to contribute to the top-down process of transmission and regulation of pain from the cortical and limbic areas in the brain to the dorsal horns of the spine. Research on how structures and functions are altered in the event of CP is still lacking ^[178], but there are a few aspects that have supporting evidence in literature.

The periaqueductal grey (PAG) in the midbrain and the rostral ventromedial medulla (RVM) have been proven to be involved in the descending modulation system ^[20, 178, 179]. These two centers contain a high number of opioid receptors and endogenous opioids. Descending pathways are connected with the dorsal horns, where they project neuro-signals which modulate pain transmission. These pathways utilize noradrenaline and serotonin as neurotransmitters.

The descending pathways use two modulatory mechanisms: inhibitory and stimulatory. Both mechanisms need to be involved and balanced for the experience of pain to be healthy and functional ^[20] (that is, noxious experience proportionate to the stimulus). It appears that an imbalance between these two systems is one contributing factor that triggers acute pain to become chronic ^[170]. Both of these functions appear to be regulated by the PAG; located in the brainstem, the PAG projects to the rostroventral medulla and the spinal horns. The anatomical position of such an important modulatory component of the brain puts into evidence that the whole CNS is involved in the modulation of pain and possibly in the mechanisms behind chronicity. These findings point to a new area of research to be performed.

A 2014 study ^[180] provides evidence on how brain areas connected to the PAG change in patients affected by chronic low back pain. The results of this study highlight neuroplasticity as part of the development of chronic pain, in particular as a mechanism necessary for the body to adapt to the pain.

2.1.3.2.2 Ascending

Ascending modulatory pathways are deeply interconnected with descending pathways in the regulation of nociception. The regulatory mechanisms in this case are based on positive and negative feedback loops.

The best example of this mechanism is the renowned “Gate Control Theory”. This theory explains how the activation of non-nociceptive neurons may interfere with the transmission of nociceptive stimulus that was simultaneously evoked in the same spinal tract area, by the activation of specific modulatory and

inhibitory cells in the spine. The same theory also illustrates the modulatory process involving the descending pathways. Certain neural tracts bypass the spinal modulatory and inhibitory “gate” reaching the brain directly, and activating the descending modulatory pathways that further contributes in the modulation of pain.

The complexity of these mechanisms has not been sufficiently studied and it is not fully understood.

2.1.4 Inflammation

2.1.4.1 Introduction

Inflammation and sub-inflammation have been increasingly pointed as possible underlying causes for a large number of chronic conditions. Since chronic diseases account for the largest portion of pathologies affecting wealthier societies (as high as 70%) ^[181], there is increasing attention from the scientific community to studying the relationship between inflammation and chronic conditions, as well as their possible causes and association. Particularly, one aspect of chronicity that has been extensively researched is the link between chronic sub-inflammation (measured by heightened blood levels of C-Reactive Protein, a widely used inflammatory marker) and the incidence of cardiovascular diseases (CVD) ^[182-185]. More specifically, there is evidence that higher C-Reactive Protein (CRP) levels are related to increased incidence of coronary heart disease (CHD) ^[186]. Other markers (e.g. interleukin 6 (IL-6) levels ^[34] and homocysteine levels ^[59]) have been studied as well, and there is evidence for their contribution to atherosclerosis and CVD. These markers have all been described in the review authored by Stoner et al. ^[187].

The demonstrated association ^[188] between inflammation and CVD is only one of many examples on how inflammation is connected to chronic conditions. Other diseases associated with chronic inflammation include: osteoarthritis ^[189], metabolic syndrome and insulin resistance ^[39], cirrhosis ^[26], asthma ^[34], rheumatoid arthritis ^[190], different cancers ^[31, 32, 59, 191, 192] and even depression ^[193]. The associations are so vast in number that various authors have hypothesized that western lifestyle itself (with a pool of different contributing factors including diet, stress, pollution and lack of daily physical activity) could be the leading cause of chronic conditions ^[194].

Even though inflammation and sub-inflammation have been found to be very important as a pathologic cause to many chronic conditions, a scarce amount of literature could be found on the direct link between inflammation and chronic pain.

2.1.4.2 Inflammation and chronic pain

Of vital importance for this study is the link between inflammation or sub-inflammation and sensitivity to pain as well as the number of sites where the pain is located. Afari et al. ^[195] found that higher levels of CRP are associated with an increased pain sensitivity (both in regards to threshold levels and tolerance). Additionally, Lee et al. ^[196] found that CRP levels are inversely related to pain threshold at the wrist, which means that higher CRP levels (and therefore higher inflammation levels) meant it was easier for the study subjects to experience pain.

Generaal et al. ^[21] found that markers for basal inflammation were higher in patients with chronic multisite pain when compared to controls, although the statistical significance was lost after adjustment for different covariates. In that study

^[21], the multisite pain group versus the controls was defined as three sites or more. This arbitrary cut-off might have decreased the significance of the systemic effect that basal inflammation has as a possible underlying cause for multiple pain sites. The presence of two pain sites might indicate that a systemic process is already underway ^[197].

Another study by Li et al. ^[198] provides a good explanation on the role of neuroinflammatory patterns as contributors to chronic pain, and also as a possible route for treating such pain. In another very recent study, Lasselín et al. ^[27] point out that low-grade inflammation may have an adverse effect on the outcome of behavioral treatment used for treating chronic pain in adults.

In a 2015 study ^[58], substance P serum concentration was found to be positively correlated with chronic pain intensity levels when analyzing individuals affected by rheumatoid arthritis (RA, a systemic auto-immune inflammatory-mediated condition causing joint pain) and individuals affected by osteoarthritis (OA, a degenerative condition which causes joint pain, mediated by local inflammation). Substance P concentration was elevated in both groups, although significantly different between the two groups, and higher in the RA group. This finding stresses the important role of the inflammation process in both of these painful conditions, and also highlights a connection between autoimmune diseases, systemic chronic inflammation, and pain levels. Overall, this study points out that inflammation level is associated with chronic pain levels.

2.2 Diet and inflammation

2.2.1 Diet-related effects on human body

The focus of this research was to study the effects of diet on the human body in a context to better understand the impact of inflammation on human health. A particular emphasis has been placed on inflammation, diet, chronic pain, and how these factors interact with each other. These interactions have been researched in the literature and reviewed.

Research on dietary-mediated physiological responses has shown relevant associations with a broad spectrum of chronic conditions, mediated by a variety of different mechanisms ^[199]. These physiological responses include inflammatory and sub-inflammatory states ^[39, 41], oxidative state ^[200, 201], immune response ^[202, 203], DNA methylation level ^[35, 42], insulin resistance ^[38, 204], and blood fat levels ^[205, 206]. A complete list of all dietary-mediated physiological markers associated with these responses and found in literature is listed in Figure 1.

From the literature review of the above-mentioned physiological responses, sub-inflammatory states ^[27, 207], oxidative state ^[208, 209], immune response ^[207, 210], and DNA methylation level ^[211, 212] were found to be associated with CP. These associations are discussed later in this chapter (section 2.3). A mediating link between these associations and diet could not be found in current literature ^(note 1).

Studies on the association between chronic pain and either higher blood fat levels or insulin resistance were not found in literature. Nonetheless, both higher blood fat levels and insulin resistance are associated with other chronic conditions, such as chronic migraine ^[213] and central obesity ^[214]. Research on insulin resistance

and blood fat levels in association with CP could not be found in current literature as well.

Figure 1: Inflammatory markers related to diet.

Inflammation markers related to diet: Advanced glycation end products (AGEs) Angiotensin II (ANG II) E-selectin Heat shock protein (HSPs) Matrix metalloproteinases (MMPs) Myeloperoxidase (MPO) Platelet endothelial cell adhesion molecule-1 (PECAM-1) Intracellular cell-adhesion molecule-1 (ICAM-1) Vascular cell adhesion molecule-1 (VCAM-1)	Oxidized LDL (oxLDL) Cytokines related to diet: CD40/CD40L C-reactive protein (CRP) Interferon-gamma (IFN- γ) Interleukin-1 (IL-1) Interleukin (IL-6) Tumor necrosis factor- α (TNF- α)
Oxidative stress biomarkers related to diet: Isoprostanes Lipoprotein-associated phospholipase A2 (Lp-PLA2) Nitrotyrosine	Chemokines related to diet: Interlukin-8 (IL-8) Monocyte chemoattractant-1 (MCP-1) Migration inhibitory factor (MIF)

2.2.2 Dietary pattern and inflammation

The associations between diet and inflammation have been increasingly pointed out in recent literature ^[28]. From the review performed for this study, two main tools were found for evaluating the diet-related inflammation level in individuals. The first tool is known as the Dietary Pattern (DP) and the second one is the Dietary Inflammatory Index (DII). In this section of this study, DP literature

findings relevant to the interaction between diet and inflammation were evaluated. Section 2.2.3 is dedicated to the findings on diet-related inflammation as related to the DII.

The Dietary Pattern approach takes into account the overall effects from each specific combination of nutrients and foods that are part of one's individual diet. This is in opposition to other studies that focus on a limited number of specific nutrients or foods consumed. For the purpose of understanding the overall effect of diet, the Dietary Pattern approach offers a valid and thorough approach ^[215].

Specific DPs have been associated with higher inflammation levels in the body and have shown interesting connections with chronic conditions, which make them relevant to understand how diet-related inflammation affects the human body. DPs that have been consistently associated with higher levels of inflammatory markers share some aspects. For example, Western DP ^[39, 40], meat DP ^[36], sugar DP ^[36], southern cone (of Latin America) DP ^[43] and bar DP ^[216] are all characterized by higher meat consumption, decreased vegetables and fruits consumption, as well as higher consumption of refined sugars and grains.

An anti-inflammatory DP has been consistently found in the above mentioned studies and is usually called “prudent” ^[217, 218]. It is characterized by a higher consumption of vegetables, fruits, and whole grains along with a reduced intake of processed meat, refined sugars, and white wheat flour. Another DP, known as “Mediterranean”, shares similar food consumptions with the “prudent” one. These findings help illuminate what pro-inflammatory or anti-inflammatory diets look like.

Chronic conditions were found to be associated with pro-inflammatory dietary patterns include type 2 diabetes ^[219-221], cognitive decline ^[222], decreased

endothelial function ^[223], higher risk of depression ^[224], and metabolic syndrome ^[220].

No study could be found on the association between DP and CP.

2.2.3 DII and inflammation

The DII has been used for the diet-related analysis in this manuscript. The DII has been developed using a comprehensive review on inflammation and diet, and since its development, a wide body of literature has been produced using this tool. For these reasons it has been chosen for this work.

2.2.3.1 DII construction

The DII is a relatively recent (2014) and validated tool ^[37] for analyzing the level of inflammation that specific foods and nutrients contribute. These food and nutrients have been selected from an extensive review of 1943 articles, which resulted in 11 food consumption datasets that apply to 11 different areas and populations around the world. The analysis that led to these results looked at the association between six inflammatory biomarkers (IL-1 β , IL-4, IL-6, IL-10, TNF α and CRP) and 45 specific food items.

For each of the 45 foods, a specific value of +1, -1, and 0 was given (pro-inflammatory, anti-inflammatory, and null respectively). This value was then weighted according to the number of articles found and their design (better quality designs yielding more weight). An overall calculation was then made for each food, subtracting the anti-inflammatory values from the pro-inflammatory values to obtain a single, overall score for each food. Examples of these food components are different

vitamins (A, B6, B12, C, D, E), minerals (Fe, Mg, Se, Zn), macronutrients (protein, fats, carbohydrates), and spices (saffron, thyme, pepper, turmeric).

The 24 hours' food frequency questionnaire helped collect data on quantity and frequency of these foods. The calculation of the DII was then made based on quantity and frequency of consumption for each of the 45 specific food item values found in the review, although frequently the foods identified in questionnaires yield data only on 25-30 food items. The final DII score for each person represents the sum of the identified items' values calculated relative to the global diet dataset. This final score represents the overall tendency of one's diet to be pro-inflammatory or anti-inflammatory.

A more technical description of the calculation process for the DII is presented in the following chapter.

2.2.3.2 DII known effects

The DII has been utilized increasingly since its creation in 2014. From a literature search, 58 articles with “Dietary Inflammatory Index” in the title are present.

DII scores representative of pro-inflammatory diets have been associated with a variety of physiological changes and conditions. Among the physiological changes associated with a pro-inflammatory DII score are higher levels of a variety of inflammatory markers ^[225] (CPR ^[44, 226], TNF- α , IL-1, IL-2, IFN- γ and VCAM ^[227], and IL-6 ^[34]), shorter telomere length ^[226, 228], decreased bone mineral density ^[229], and decreased lung function (assessed with FEV1) ^[34].

Regarding conditions associated with pro-inflammatory scores of DII, current literature suggests a negative association with insulin resistance, fasting glucose and post load glucose ^[230, 231], a heightened risk of asthma ^[34], a lengthier hospitalization time for surgically-treated colorectal cancer patients ^[232], presence of metabolic syndrome ^[225, 233-235], higher risk of developing certain cancers (colorectal ^[32, 60, 192, 236], prostatic ^[59], pancreatic ^[31], ovarian ^[237, 238], breast ^[239], gastric ^[240], bladder ^[241], and lung ^[242]), higher indices of obesity ^[61], higher incidence of cardiovascular diseases ^[228, 234, 243-247], depression ^[245, 248], increased all-cause mortality ^[234, 246], decreased long term cognitive function ^[249], and increased risk of developing Multiple Sclerosis ^[250]. Current research on the association between DII and chronic pain could not be found in the literature.

2.3 Other possible mediating mechanisms between CP and diet

Inflammation is not the only possible mediating cause between CP and diet. At least four other possible mechanisms have been identified in the literature. Those mechanisms are described in the following sections.

Blood fat levels and insulin resistance have yet to be specifically researched as possible contributing factors to chronic pain, but both are associated with other chronic conditions, such as chronic migraine ^[213] and central obesity ^[214].

2.3.1 Immune response, diet, and chronic pain.

Generaal's study ^[21] pointed out that an increased response from the immune system might be further studied as a "potential biomarker for onset and perpetuation of chronic pain" (p. 1610). This is a very important perspective addressed by other authors as well and it suggests a multifactorial understanding of chronic pain. In 2004, Serhan and Chiang wrote a review on "resoleomics" ^[251] (a term which Serhan created in 1996). This neologism means the "systematic analysis of the resolution phase of inflammation using combined proteomics, lipidomics, and genomics to establish the temporal relationship of the key components to homeostasis" (p.69). In particular, the authors shed light on the role of the immune system in the inflammatory resolution process, putting a great emphasis on evidence for the complexity and multiple factors which interconnect the immune system and the inflammatory process and which were previously unknown. According to these new findings, the inflammatory process should not be viewed as a mere "passive" resolution of a stressful local event, but rather as the dynamic orchestration of the whole immune system - and, therefore, of the entire body. This understanding is critical in relation to this study when considering that specific dietary patterns which are considered "anti-inflammatory" (i.e., the fruits and vegetables rich dietary pattern, "Mediterranean dietary pattern", gluten free diet, and n-3 fatty acid enhanced diet) have been shown to have a protective effect on the immune system or even enhance its performance ^[252-255]. On the other hand, a protein and carbohydrate-rich diet, or the "Western dietary pattern", which has been shown to be "pro-inflammatory", has also been shown to heighten the reactivity of the immune system, and potentially predispose patients to autoimmune diseases ^[203, 256].

2.3.2 DNA methylation pattern, diet and chronic pain.

A direct link between DNA methylation pattern and pain has been shown in two different studies. The study by Tajerian et al. ^[211] demonstrated a link between lower DNA methylation levels and low back pain, while Doebling et al. ^[212] revealed that opioid-induced DNA methylation might be linked to at least part of the painkiller effect of opioids. Furthermore, DNA hypomethylation is associated with dietary patterns poor in fruits and vegetables, and is believed to be a predisposing factor for certain cancers ^[257]. In contrast, the Mediterranean diet has been associated with relief in the oxidative stress of the body and an enhanced ability for DNA repair ^[258]. Lastly, a lower methylation pattern has been associated with a higher peripheral presence of blood mononuclear cells ^[259], which consist of lymphocytes (T cells, B cells, NK cells) and monocytes. More research needs to be done in this area to clarify the role of DNA methylation as a possible linking mechanism between chronic pain, diet, immune response and inflammatory response.

2.3.3 Gut microbiota, inflammation, diet, and chronic pain.

A possible mediating mechanism between diet and inflammation may involve the gut microbiota. Studies have shown that dietary patterns influence the lower digestive system state of inflammation by affecting the gut microbiota ^[62, 63] and by creating a local immune inflammatory-type response ^[64, 65], which can then become chronic and systemic ^[66]. This means that a systemic inflammation might

cause a multi-systemic sensitizing effect which can then lead acute pain to become chronic.

Only one study could be found on the interaction between a decreased level of gut microbiota strains and the presence of chronic pelvic pain syndrome ^[260]. This interaction was strong, to the extent that the authors pointed out that the gut microbiota could not be only a biomarker for assessing the chronic pelvic pain syndrome, but also a potential therapeutic target in addressing the condition. These results open up an interesting perspective on the interaction between gut microbiota and chronic pain, although more research is needed in the area.

2.3.4 Oxidative state, diet, and chronic pain.

Oxidative state has been associated with conditions characterized by chronic pain, such as chronic fatigue syndrome ^[261-263], fibromyalgia ^[264-266], and chronic daily headaches ^[267]. The mechanisms mediating this association are still unclear.

A few studies point to specific dietary components ^[201], as well as anti-oxidative supplements ^[261], to promote a decrease in the oxidative status, although the research in this area is still limited to very few studies. Scientific articles investigating a direct link between diet and oxidative state could not be found in current literature.

Note 1.

Literature research was performed on PubMed, PubMed Health, and PMC in May 2015 (and lastly updated in Dec 2016) using

the following combinations of key words:

- inflammation AND diet AND chronic pain
- sub-inflammation AND diet AND chronic pain
- Chronic inflammation AND diet AND chronic pain
- Oxidative state AND diet AND chronic pain
- Immune response AND diet AND chronic pain
- DNA methylation levels AND dietary intake AND chronic pain
- inflammation AND dietary intake AND chronic pain
- sub-inflammation AND dietary intake AND chronic pain
- Chronic inflammation AND dietary intake AND chronic pain
- Oxidative state AND dietary intake AND chronic pain
- Immune response AND dietary intake AND chronic pain
- DNA methylation levels AND dietary intake AND chronic pain

CHAPTER 3: METHODS

3.1 Data source

3.1.1 The NHANES dataset description

The present study implements a cross-sectional design using the 2003-2004 National Health and Nutrition Examination Survey (NHANES) sample population.

The 2003-2004 National Health and Nutrition Examination Survey (NHANES) dataset was used for this study. The NHANES is an ongoing program of data collection, research and studies for the United States that aims to assess the Health and Nutrition status of the general U.S. population. The unique aspect of this broad survey is the combination of data collection methods, which happens both through interviews and physical examination. The NHANES program is conducted by the National Center for Health Statistics (NCHS), which is a department of the Centers for Disease Control and Prevention (CDC), the U.S. Public Health Service Agency. The NCHS was appointed by the CDC to keep statistical records of the U.S. population through recurrent surveys. This particular survey began in 1959 (under the name of NHES - National Health Examination Survey) as a way to assess for chronic conditions. It has been adapted to the changing needs of relevant information for the U.S. and its scientific community.

Data were collected over two years: each year from approximately 5,000 participants across 15 U.S. counties (different each year), for a total of approximately

10,000 individuals and 30 counties. The data were then combined for analysis. Data from participants were collected in two distinct ways: health interviews were conducted in the participants' homes, and physical examinations were done in special Mobile Examination Centers (MEC) specifically located in areas of interest. Interviewers, a significant portion of whom were bilingual, included physicians, dentists, medical technicians, health technicians, and dietary and health interviewers. Not every participant was administered an interview and a physical exam, though all were offered. Some participants declined one component or the other. The unweighted response rate for the interviewed sample was 79%, while for the examined sample was 76%.

For both modalities, data were collected electronically and stored into databases. Patients were given privacy to answer sensitive questions; in these cases, interviewers were not allowed to see the answer, which was directly typed into the computer.

A comprehensive questionnaire was handed to the participants, and included sections on demographics, diet, health status, occupation, insurance coverage, physical activity and medications taken. Two portions of this questionnaire were relevant to this study: the "24HR dietary recall" section and the "miscellaneous pain" section. These portions were handed out on the first day (day 1) in the Mobile Examination Center (MEC), or at home for those who agreed only to the interview. A second "24HR dietary recall" was administered via phone in a window of time between 3 to 10 days after the first one was completed. Most participants (87%) have two days of complete intakes.

Patients were contacted via mail, and transportation was provided to facilitate participation in the study. Participants were given compensation for their time. Privacy was strictly kept at the time of data collection for all information and data collected, and it is still currently maintained.

Datasets from NHANES are available on the CDC website ^[68] and can be downloaded and used freely (except certain sensitive variables data which were not used for this study). The response rate of the dataset was 79% in the interviewed sample and 76% in the examined sample.

3.1.2 Stages of the NHANES dataset selection process

The sample set is a stratified multistage probability selection of the civilian non-institutionalized population of the United States. Adolescents (15-19) and people over 60 years were oversampled, as well as African Americans and Mexican Americans, to validly estimate these groups. The NHANES procedure to recruit the sample set consists of the following four stages.

3.1.2.1 Stage 1 – County selection

Single counties or groups of contiguous counties were selected. Different strata were defined according to geography and proportions of minority groups in the involved areas. From these strata (counties), Primary Sampling Units (PSUs) were then selected. In the majority of cases, there were two PSUs per strata.

The method used for the calculation of the distribution across minorities was the proportional to a measured size (PPS) to ensure proper representation in the final dataset.

3.1.2.2 Stage 2 – Spatial Allocation

The PSUs were organized into different segments based on spatial allocation (i.e., city blocks). Again, the method used for the calculation of probability of these sample segments was PPS.

3.1.2.3 Stage 3 – Household selection

Households were randomly selected from each segment highlighted in stage 2. This process was performed respecting the predefined parameters of oversampling, wherever necessary.

3.1.2.4 Stage 4 – Individuals' selection

Individuals were again randomly selected within the predefined age-sex-race/ethnicity sub-domains. These people were selected from each of the households selected in stage 3. On average, 1.6 persons were selected per household.

3.1.3 Study sample selection process

3.1.3.1 Inclusion and exclusion criteria

The first inclusion criterion imposed for the selection of individuals from the dataset was age (ages 20 to 85 were included). This criterion was applied for two

reasons. First, the study was designed to target the adult population. Second, only individuals between the ages of 20 and 85 have pain variables data reported, while data for the 24HR dietary recall is available for individuals between 6 and 85 years of age. Therefore, only the age span of 20 to 85 was included in this analysis.

The other criterion was the presence of data on both the relevant pain variables and on the dietary intake, where the latter had to be collected during both interview sessions. Only individuals with data collected on both variables were included, and if data was missing on either variable, the individual sample was excluded from this analysis. Only individuals with dietary intake data collected in both occasions of the questionnaire administration were included, to provide more reliable information on the intrapersonal variability of diet.

3.1.3.2 Inclusion and exclusion criteria application

The initial selection for the sample population included 12,761 individuals, with age ranging from 0 to 85. Among these subjects, 10,122 were interviewed (79.3 percent), and 9,643 (75.6 percent) were given the medical exam. For the purpose of this study, all those who received the interview were considered initially.

Upon applying the first inclusion criteria (subject age 20 to 85), the sample population size was reduced from 10,122 to 4,818. Within this age-selected population, only 3,966 individuals had data on both dietary intake and chronic pain. These 3,966 individuals were the study population dataset.

An additional inclusion criterion was imposed for the tertiary variable of pain duration. To be included in this analysis, an individual had to have responded

“yes” to the secondary variable question (“in the past month, did you have pain lasting longer than 24 hours?”). This last criterion matched for 1,033 individuals in the dataset.

3.2 Study Variables

3.2.1 Dependent variables

The main outcome (dependent) variable was the presence or absence (dichotomous variable) of pain during the three months preceding data collection in the neck and/or lower back. This definition is comparable to the commonly accepted definition of chronic pain from the International Association for the Study of Pain (IASP), which is “pain which has persisted beyond normal tissue healing time”. If no other criteria are specified, usually that amount of time is considered to be three months ^[268]. In the IASP definition, the frequency and consistency of pain during this period of time are not specified (e.g., it is not specified if the pain needs to be present every day, or the majority of days, or if it should just be a recurring pain in the same area). The question asked in the questionnaire (“During the past 3 months, did you have neck pain?”) covers the proper amount of time, although it does not clarify the exact extent of the pain duration. Further instruction in the question explanation states “the following questions are about pain you may have experienced in the past 3 months. Please refer to pain that lasted a whole day or more. Do not report aches and pains that were fleeting or minor”. This indication leaves space for interpretation and is a possible source of bias.

A secondary dependent variable, namely, the presence or absence (dichotomous variable) of pain lasting more than 24 hours during the month preceding the interview, was categorized and analyzed as well. This analysis was made to help frame the type of pain described in the main outcome variable. A scenario where pain lasted more than 24 hours was anticipated to support a situation where pain leans more towards chronicity.

To further investigate this hypothesis, a tertiary analysis was done on the subpopulation of people who responded “yes” to having pain lasting longer than 24 hours in the preceding month. This subpopulation accounted for 1033 individuals. The data available for these individuals were divided into four categories: pain lasting less than a month, pain present for at least 1 month but less than 3 months, pain for at least 3 months but less than 1 year, and pain presence for a period greater than 1 year. These categories were collapsed into a dichotomous variable (pain up to three months and pain longer than three months) and treated accordingly. The decision for collapsing the four categories into two was made based on the clinical relevance of the time frame in the definition of chronic pain.

The variables derived from this questionnaire are coded under the name of “miscellaneous pain” (MPQ_C). “Miscellaneous pain” is a group of questions administered during the interviewing process. It includes 12 different questions on pain (duration, intensity, location, and frequency). The four questions considered for this research were coded as question MPQ.060 (pain in the lower back), MPQ.070 (pain in the neck), MPQ100 (pain lasting longer than 24 hours), and MPQ110 (pain duration). Question MPQ.060 and MPQ.070 were merged into one variable (pain either in low back, or neck, or both, versus no pain), while question MPQ100, and

MPQ110 were merged into a different variable (pain lasting up to three months or longer than 3 months). A total of 5411 individuals provided information about their pain history.

3.2.2 Main exposure variable

The main exposure variable was DII, which was treated as a continuous variable in the study. The DII was calculated from the raw data available from the Food Frequency Questionnaire based on the method described by Shivappa et al. ^[31, 32, 37, 44, 59], and discussed in section 2.2.3.1 and further in this section.

The data used to calculate the DII were collected as part of the questionnaire (“24HR dietary recall”) that was handed out the first day (day 1) in the Mobile Examination Center (MEC), or at home for those who agreed to the interview only. A second “24HR dietary recall” questionnaire was administered via phone in a window of time between 3 to 10 days after the first one was completed. Most participants (87 percent) had 2 days of complete intakes.

Calculation of the DII was made based on quantity and frequency of consumption of 28 specific food item values. In the original review, 45 items were recognized, but, in line with previous researchers ^[32, 34], a lower number (28) of items were analyzed. The included food items were identified from the questionnaire as matching those from the “golden standard” values coming from the original literature review performed to construct the DII in 2014. More specifically, the DII has been calculated by first linking the dietary data to one of the 11 regionally representative world databases (described in section 2.2.3.1), which are based on different diets highlighted from the systematic review. This systematic review provides a mean and

standard deviation for each food parameter ^[37], which is considered the “standard global mean”.

The “standard global mean” was then subtracted from the individual's value of each food item consumption recorded (the data registered with the questionnaire) and divided by the standard deviation. The individual food item consumption was calculated by averaging the mean of the total Nutrient Intakes (File Coded as DR1TOT_C and DR2TOT_C) for the nutrients of interest from the two days of collection.

These data were converted to a centered percentile to avoid the common occurrence (for dietary data analysis) of “right skewing”. This phenomenon describes a positive skewing, resulting in a longer right tail on the distribution curve, and which requires advanced statistical measurements to analyze appropriately. In order to avoid complicated analysis, the data were converted to a centered percentile. The centered percentile was then multiplied by the effect score (gathered for each specific food in the literature review ³⁷). This method provides a DII score that is parameter-specific for the individual.

The final DII score for each person represents the sum of the 28 items' value calculated for each individual relative to the global diet dataset. This value represents the overall tendency of one's diet to be pro-inflammatory or anti-inflammatory. In line with previous studies, the value of this variable was between -7.5 (diet overall anti-inflammatory) and +8.5 (diet overall pro-inflammatory). For the purpose of statistical analysis, the DII was treated as a continuous variable, based on current literature findings ^[33, 269-271].

The independent variable contains the most data entries, a total amount of

9,643, although only 9,034 provided completed data. Of this figure, only 8,354 individuals completed both days' interviews.

3.2.3 Covariates

Based on literature review ^[21, 46, 55, 193, 199, 211, 212, 214, 272-283], many relevant and consistent confounders related to pain and sub-inflammation collected in the survey were examined. The following possible confounders were investigated: age ^[284], gender ^[285], BMI ^[286], physical activity level ^[287], education level ^[55], diagnosis of diabetes ^[288], race/ethnicity ^[289], general health condition ^[290], total annual income ^[291], marital status ^[292], number of people per household ^[293], and insurance cover ^[199].

Age (calculated in months), and BMI (calculated as height/weight; in cm and kg) were treated as continuous variables. The other variables were categorical and were treated as described here. Physical activity level was divided into four levels: 1- sit much during the day and do not walk much; 2- stand or walk about a lot during the day, but do not have to carry or lift things very often; 3- lift light load or climb stairs or hills often; 4- perform heavy work or carry heavy loads. Sex was divided into male and female. Education level was divided into three groups: 1- less than high school diploma; 2- high school diploma; 3- more than high school diploma. Diagnosis of diabetes was classified into three categories: 1- yes, 2- no, and 3- borderline according to the question "did your doctor tell you that you have diabetes?". Race/ethnicity was divided into five groups: 1- Mexican American, 2- Other Hispanic, 3- White Non-Hispanic, 4- Black Non-Hispanic, 5- Other Race (which includes multi-racial). General health condition was divided into five groups as well: 1- excellent, 2- very good, 3- good, 4- fair, 5 -poor. Total Annual Household Income was divided into four

groups: 1- up to 20,000\$/year; 2- up to 45,000\$/year; 3- up to 75,000\$/year; 4- over 75,000\$/year. Marital status was divided into two groups, 1- married / living with a partner and 2- never married, separated, divorced, widowed. Number of people per household was divided into 5 categories: 1- one, 2- two, 3- three, 4- four and 5- five or more people living in the household. Insurance coverage was dichotomized into yes/no.

Other known confounders (e.g., smoking status) were not considered due to the high number of missing values.

3.3 Statistical analysis

The statistical software used for all analyses was SAS 9.4 for Windows (SAS Institute Inc., Cary, NC, USA).

3.3.1 Population baseline characteristics

Baseline characterization of the population over 20 years old of age was made to compare the included individuals who had dietary information available and the excluded individuals who did not have the dietary information available.

Pearson's χ^2 test was used to compare the baseline characteristics for the categorical variables (gender, physical activity level, education level, diagnosis of diabetes, race/ethnicity, general health condition, annual income, marital status, number of people per household, and insurance cover). The t-test was used to compare the baseline characteristics for the continuous variables (age and BMI).

3.3.2 Sample weight for dietary intake data

The population data selected for this study were analyzed through complex probability sample, and sample weight information provided with the NHANES dataset was utilized in all analyses, including descriptive analysis. Description of the weight rules used in this population data analysis is in the following paragraph.

The majority of the 2003-2004 NHANES dataset is designed to be analyzed using the weight for data collected in the MEC centers (weight code: WTMEC2YR). When it comes to dietary data though, the weights to be used are different. This difference depends on the fact that data were collected disproportionately more during weekends, which would cause an underrepresentation of food consumed during week days versus food consumed during weekends. This is based on the understanding that food is consumed differently in different days of the week.

To overcome this sampling bias, there are two different weights provided with the dataset designed to be used when performing statistical analysis on dietary variables. A specific weight (WTDRD1) has been calculated for individuals who answered only the first of the two 24HR questionnaires. This weight was constructed using the MEC sample weight (WTMEC2TR), and adjusted for (1) additional non-response, and (2) different day-of-the-week allocation for the dietary intake data collection. This weight has no direct application for this study, since the inclusion criteria allow only data from individuals with information from both interviews.

The weight that was used for this study was another specific weight, coded WTDR2D. This two-day weight was constructed for the 8,354 respondents

who entered valid data from the two recalls. This weight is calculated by taking the Day 1 weights (WTDRD1) and computing an adjustment for (1) additional non-response for the second recall and (2) the proportion of combinations of different days of the week for Day 1 and Day 2 recalls.

The WTDR2D sampling weight was applied in all statistical analysis including descriptive, univariate, and multivariate analysis. This weight has been normalized through the following process: first, the average of all the survey weights from all analyzed units was calculated; then, the survey weight of each unit used in the analysis was divided by that average. Bootstrap weights were not used for this study. The SAS command used for this computation was PROC LOGISTIC with the addition of the command WEIGHT, followed by the name of the normalized weight variable.

3.3.3 Dietary Inflammatory Index and Neck/Low back pain (main outcome variable)

The main exposure variable (DII) was tested as a continuous variable. The main outcome variable, presence/absence of chronic pain in the neck and/or lower back, was treated as a dichotomous variable.

A logistic regression model was used to identify the significant factors associated with chronic pain. Odds Ratio and 95% CI were calculated. All covariates were tested for interaction as effect modifiers as well as confounders.

3.3.4 Dietary Inflammatory Index and pain lasting more than 24hr over a one-month period (secondary outcome variable)

The independent continuous variable of DII was tested against the dependent dichotomous variable of presence/absence of any pain present for more than 24hr over the month before the interview.

A logistic regression model was used to identify the significant factors associated with chronic pain. Odds Ratio and 95% CI were calculated for the regression model. All covariates were tested for interaction as effect modifiers as well as confounders.

3.3.5 Dietary Inflammatory Index and pain duration (tertiary outcome variable)

The independent continuous variable of DII was tested against the dependent dichotomous variable of pain lasting less than three months versus pain lasting longer than three months.

A logistic regression model was used to identify the significant factors associated with chronic pain. Odds Ratio and 95% CI were calculated for the regression model. All covariates were tested for interaction as effect modifiers as well as confounders.

3.3.6 Final Model construction

The final model construction initially included all the variables which were deemed significant in the univariate analysis at $\alpha=0.20$. The final model construction was then performed using a manual method, and a likelihood ratio test for significant difference was conducted. One at a time, all the non-significant variables ($p>.05$) were removed, by taking away one at the time the least significant, until a significant difference in the model was detected. All the included variables were tested for interaction and possible confounding effect. The threshold for detecting a significant change in the main effect variable (beta coefficient) when removing covariates from the model was set at 20%. All the continuous variables were also assessed for linearity by testing for correlation between dependent variable and independent variables. Outliers were assessed for with Cook's method. Model fit was test with Hosmer and Lameshow's diagnostic plots.

CHAPTER 4: RESULTS

4.1 Baseline characteristics analysis

4.1.1 Included vs. excluded population >20yrs old.

An analysis of the baseline characteristics of the included (3,966 participants) versus excluded (848 participants) populations over 20 years old was performed (Table 1). There were no significant differences in diagnosis of diabetes, self-reported general health condition, and mean age between the two groups. Significant differences were found in the other confounders.

The included population had a significantly higher number of women and a higher prevalence of education level greater than high school when compared with the excluded population. Analysis to the variable of physical activity level performed each day showed that the included population had a lower prevalence of heavy workers, compared to any other activity level assessed. A higher prevalence of married people was observed in the included population, and race/ethnicity for the included population had a higher prevalence of non-Hispanic white, and a lower prevalence of non-Hispanic black and other ethnicities compared with the excluded population. The variable of number of people per household showed that the included population had a higher prevalence of 2 people per household compared to any other household size. The included population had a higher rate of insurance coverage compared to the excluded population. Annual income for the included population was

higher than the excluded population, with a higher prevalence of income over 45.000\$/year. Lastly, BMI mean was higher in the included population.

Table 1. Baseline characteristics of included versus excluded population (> 20yrs old). (Note that missing values are not specified if not present).

Baseline characteristics (population >20 years old) (* = Significant value)		Excluded population n=848 (%)	Included population n=3966 (%)	p-value
<u>Gender</u>				
	Male	51.80	47.43	0.0255*
	Female	48.20	52.57	
<u>Education level</u>				
	Less Than High School	47.46	16.76	<.0001*
	High School Diploma	28.12	26.72	
	More Than High School	23.78	56.49	
	Missing	0.64	0.04	
<u>Level of daily physical activity</u>				
	Sit during the day and do not walk about very much	25.47	24.01	0.0005*
	Walk a lot during the day, do not carry or lift things very often	49.55	51.11	
	Lift light load or have to climb stairs or hills often	13.45	17.33	
	Do heavy work or carry heavy loads	11.51	7.49	
	Missing	0.02	0.06	
<u>Diabetes</u>				
	Yes	7.12	7.82	0.7922
	No	91.69	91.04	
	Borderline	1.20	1.14	

<u>Marital status</u>				
Married or living with a partner	54.21	65.67		
Widowed, divorced, separated, never married	45.30	34.26	<.0001*	
Missing	0.48	0.07		
<u>Race/Ethnicity</u>				
Mexican American	8.55	7.72		
Other Hispanic	3.13	3.77		
Non-Hispanic White	63.57	73.15	<.0001*	
Non-Hispanic Black	14.86	10.56		
Other Race – Including Multi-Racial	9.89	4.79		
<u>Number of people per household</u>				
1	18.94	12.29		
2	28.22	36.18		
3	19.83	18.02	<.0001*	
4	18.60	16.64		
5+	14.42	16.86		
<u>Insurance cover</u>				
Yes	72.90	82.22		
No	23.55	17.15	<.0001*	
Missing	3.55	0.64		
<u>General health condition</u>				
Excellent	20.19	21.47		
Very good	25.89	30.25		
Good	32.71	30.91	0.0525	
Fair	16.49	13.44		
Poor	4.6	3.90		
Missing	0.09	0.04		
<u>Annual Income</u>				
up to 20.000\$/year	19.09	5.00		
20.000 to 45.000\$/year	29.86	15.89	<.0001*	
45.000 to 75.000\$/year	20.50	29.43		

	over 75.000\$/year	19.17	23.42	
	Missing	11.38	26.26	
<u>BMI</u>				
	Mean	27.19	28.41	
	95% CI	26.72 - 27.67	28.21 - 28.61	<.0001*
<u>Age</u>				
	Mean	44.9	46.3	
	95% CI	43.7 – 46.0	45.8 – 46.8	0.9686

4.1.2 Study population: individuals with CP vs. individuals without CP.

An analysis of the baseline characteristics was then performed within the included population, comparing individuals with chronic pain (n=2116) to those without chronic pain (n=1850) (summarized results shown in Table 2). This analysis shows significant differences between the two groups. These differences were found for the gender variable, where the CP population had higher women prevalence. Regarding education level, the CP population had a higher prevalence of lower than high school diploma education. The level of physical activity performed each day had a higher prevalence of both lower activity level and heavy lifting in the CP population, while non-CP population had higher prevalence of light to medium daily activity. The diagnosis of diabetes was more prevalent for the CP population. Additionally, the CP population had higher prevalence of non-Hispanic white and a lower prevalence of Mexican American. Self-reported general health condition of the lower quality categories – namely good, fair and poor had higher prevalence in the CP

population, whereas the non-CP population had higher prevalence of the very good and excellent categories. Average annual income was lower for the CP population, while BMI mean was higher for the CP population. The two populations were found to be non-significantly different in regards to marital status, number of people per household, insurance coverage, and mean age.

To control for these unbalances, the baseline characteristics that were found different in this analysis were adjusted for in the multivariate analysis performed to find the final model.

Table 2. Baseline characteristics of individuals with CP versus individual without CP in the included population. (Note that missing values are not specified if not present).

Baseline characteristics (study population) (* = Significant value)		Non-chronic pain population n= 1850 (%)	Chronic pain population n= 2116 (%)	p-value
<u>Gender</u>				
	Male	50.83	43.54	<.0001*
	Female	49.17	56.46	
<u>Education level</u>				
	Less Than High School	14.88	18.96	<.0001*
	High School Diploma	25.15	28.53	
	More Than High School	59.97	52.51	

<u>Level of daily physical activity</u>				
Sit during the day and do not walk about very much	22.77	25.41		
Walk a lot during the day, do not carry or lift things very often	52.00	50.16		
Lift light load or have to climb stairs or hills often	18.48	16.04		0.0152*
Do heavy work or carry heavy loads	6.75	8.39		
<u>Diabetes</u>				
Yes	6.26	9.61		
No	92.81	89.02		0.0002*
Borderline	0.93	1.37		
<u>Marital status</u>				
Married or living with a partner	64.89	66.70		
Widowed, divorced, separated, never married	35.11	33.30		0.2311
<u>Race/Ethnicity</u>				
Mexican American	8.54	6.82		
Other Hispanic	3.65	3.91		
Non-Hispanic White	71.35	75.17		0.0475*
Non-Hispanic Black	11.42	9.59		
Other Race – Including Multi-Racial	5.04	4.50		
<u>Number of people per household</u>				
1	11.89	12.71		
2	36.09	36.29		
3	18.36	17.64		0.8620
4	17.01	16.25		
5+	16.65	17.11		
<u>Insurance cover</u>				
Yes	82.47	81.88		
No	16.87	17.51		0.8523
Missing	0.66	0.61		

<u>General health condition</u>				
	Excellent	27.09	15.06	
	Very good	32.88	27.27	
	Good	28.84	33.25	<.0001*
	Fair	9.04	18.48	
	Poor	2.15	5.94	
<u>Annual Income</u>				
	up to 20.000\$/year	13.46	18.63	
	20.000 to 45.000\$/year	27.68	31.48	
	45.000 to 75.000\$/year	25.95	20.52	<.0001*
	over 75.000\$/year	28.38	23.85	
	Missing	4.54	5.52	
<u>BMI</u>				
	Mean	28.13	28.73	
	95% CI	27.86 - 28.39	28.43 - 29.04	0.0020*
<u>Age (in months)</u>				
	Mean	45.9	46.7	
	95% CI	45.2 – 46.5	46.0 – 47.4	0.2991

4.2 Main variable

4.2.1 Univariate analysis

Univariate analysis was conducted on each of the covariates to assess the effect of each of them on chronic pain in the lower back and in the neck (Table 3). The DII effect on the dependent variable was also assessed at this point. In this population, a significant effect on the presence of chronic pain was found for gender, education level, level of physical activity performed each day, diagnosis of diabetes, race/ethnicity, self-reported general health condition, annual income, BMI, and DII.

The DII was found to be significant with a p-value of .0099, with an OR of 1.036. To better understand this result, it is important to remember that Odds Ratios measure the unit of the variable in question. The DII ranges between -7.5 and +8.5, therefore having an overall range of 16 points. The chances of having chronic pain are 3.6% higher for every 1-point increase in the DII score. Therefore, to calculate the OR for a 3 point difference in DII score, the score difference is multiplied by the estimate “ β ” from the logistic regression ($0.0356 \times 3 = 0.1068$). The calculation of the exponential for this value ($e^{0.1068}$) gives an OR value of 1.1127. This means that a 3 points difference in the DII scale would change the odds of having chronic pain by 11.27%.

Similarly, to calculate the OR for a 9 points difference in DII score, the same calculation would be ($0.0356 \times 9 = 0.3204$); the result would then be used to calculate the exponential ($e^{0.3204}$) which gives an OR value of 1.3776. This result means that a 9 points difference in the DII scale would change the odds of having chronic pain by 37.76%.

In addition, to give an example based on the full range of the DII and calculate the OR based on a 16 points difference in DII score, the calculation would be ($0.0356 \times 16 = 0.5696$). The computation of the exponential for this value ($e^{0.5696}$) gives as a result OR= 1.7676. This means that a 16 points difference in the DII scale would change the odds of having chronic pain by 76.76%. This last result, although probably not clinically relevant, highlights the full potential of the different impact that a fully anti-inflammatory diet can have compared to a fully pro-inflammatory diet.

Table 3. Univariate analysis of covariates and DII effect on chronic pain presence

Univariate analysis: DII on CP (study population; n= 3966) (*= Significant value)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Gender</u>			
	Male	p= <.0001*	1.00
	Female		1.317 (1.158 - 1.498)*
<u>Education level</u>			
	Less Than High School	p= <.0001*	1.00
	High School Diploma		0.890 (0.729 - 1.088)
	More Than High School		0.676 (0.565 - 0.808)*
<u>Level of daily physical activity</u>			
	Sit during the day and do not walk about very much	p= 0.0174*	1.00
	Walk a lot during the day, do not carry or lift things very often		0.910 (0.695 – 1.192)
	Lift light load or have to climb stairs or hills often		0.767 (0.595 - 0.988)*
	Do heavy work or carry heavy loads		0.713 (0.537 - 0.946)*
<u>Diabetes</u>			
	Yes	p= 0.0006*	1.00
	No		0.649 (0.508 - 0.828)*
	Borderline		1.116 (0.576 - 2.159)
<u>Marital status</u>			
	Married or living with a partner	p= 0.3018	1.00
	Widowed, divorced, separated, never married		1.074 (0.938 - 1.230)
<u>Race/Ethnicity</u>			
	Mexican American	p= 0.0465*	0.748 (0.584 - 0.957)*
	Other Hispanic		1.015 (0.725 - 1.419)
	Non-Hispanic White		1.00
	Non-Hispanic Black		0.784 (0.633 - 0.970)*
	Other Race – Including Multi-Racial		0.894 (0.660 - 1.212)

<u>Number of people per household</u>			
	1		1.00
	2		1.038 (0.817 - 1.319)
	3	p= 0.9006	0.992 (0.821 - 1.198)
	4		0.949 (0.764 - 1.178)
	5+		0.932 (0.745 - 1.165)
<u>Insurance cover</u>			
	Yes		1.00
	No	p= 0.6950	0.966 (0.815 - 1.146)
<u>General health condition</u>			
	Excellent		1.00
	Very good		1.531 (1.267 - 1.850)*
	Good	p= <.0001*	2.156 (1.788 - 2.600)*
	Fair		3.780 (2.992 - 4.776)*
	Poor		5.385 (3.656 - 7.933)*
<u>Annual Income</u>			
	up to 20.000\$/year		1.00
	20.000 to 45.000\$/year	p= <.0001*	0.815 (0.671 - 0.990)*
	45.000 to 75.000\$/year		0.566 (0.461 - 0.695)*
	over 75.000\$/year		0.606 (0.496 - 0.739)*
<u>BMI</u>		p= 0.0031*	1.015 (1.005 - 1.025)*
<u>Age (in months)</u>		p= 0.0651	1.000 (1.000 - 1.001)
<u>DII</u>		p= 0.0099*	1.036 (1.009 - 1.065)*

4.2.2 Multivariate analysis

Multivariate analysis, summarized in table 4, was performed on all variables deemed significant at a .20 level in the univariate analysis. The included variables were gender, education level, level of physical activity performed each day,

diagnosis of diabetes, race/ethnicity, self-reported general health condition, annual income, BMI, and DII. In this model, the DII was found to be non-significant, with a p-level of 0.0610. Other non-significant variables were age, education level, level of physical activity performed each day, diagnosis of diabetes, race/ethnicity, and BMI.

Table 4. Multivariate analysis of covariates and DII effect on chronic pain presence – First Model

Multivariate analysis: DII on CP (study population) (* = Significant value)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Gender</u>			
	Male	p= <.0001*	1.00
	Female		1.407 (1.224 - 1.616)*
<u>Education level</u>			
	Less Than High School	p= 0. 3614	1.00
	High School Diploma		0.965 (0.772 - 1.205)
	More Than High School		0.877 (0.707 - 1.087)
<u>Level of daily physical activity</u>			
	Sit during the day and do not walk about very much	p= 0. 0457*	1.00
	Walk a lot during the day, do not carry or lift things very often		0.958 (0.809 - 1.135)*
	Lift light load or have to climb stairs or hills often		0.980 (0.790 - 1.216)*
	Do heavy work or carry heavy loads		1.417 (1.056 - 1.902)*
<u>Diabetes</u>			
	Yes	p= 0. 7634	1.00
	No		0.960 (0.730 - 1.263)
	Borderline		1.219 (0.598 - 2.487)

<u>Race/Ethnicity</u>			
	Mexican American		0.549 (0.416 - 0.725)*
	Other Hispanic		0.874 (0.612 - 1.249)
	Non-Hispanic White	p= <.0001*	1.00
	Non-Hispanic Black		0.629 (0.499 - 0.793)*
	Other Race – Including Multi-Racial		0.852 (0.620 - 1.172)
<u>General health condition</u>			
	Excellent		1.00
	Very good		1.538 (1.268 - 1.866)*
	Good	p= <.0001*	2.143 (1.756 - 2.616)*
	Fair		3.661 (2.834 - 4.730)*
	Poor		5.718 (3.717 - 8.796)*
<u>Annual Income</u>			
	up to 20.000\$/year		1.00
	20.000 to 45.000\$/year	p= 0. 0157*	0.911 (0.741 - 1.120)
	45.000 to 75.000\$/year		0.717 (0.574 - 0.895)*
	over 75.000\$/year		0.861 (0.688 - 1.079)
<u>BMI</u>		p= 0. 5355	1.004 (0.992 - 1.015)
<u>Age</u>		p= 0.2983	1.000 (0.999 - 1.000)
<u>DII</u>		p= 0. 1225	1.024 (0.994 - 1.056)

A stepwise selection method to find the best fitting model was performed with all variables included in the multivariate analysis. This procedure revealed that gender, self-reported general health condition, BMI, and DII were significant in defining a statistical model for all analyzed variables. When the multivariate analysis was run again with only these four variables considered (Table 5), DII was found to be significant, although with a weak strength (p-value= 0.0346; OR= 1.031).

Additionally, annual income was significant with a weak association (p-value = 0.0270). In contrast, gender and general health condition instead, were significant at a <.0001 level. The interaction between these four variables was analyzed by running a separate multivariate analysis for each of the possible interactions between factors, and none was found to be significant.

The DII therefore has a significant association with the presence of chronic pain when gender, general health condition, and annual income are taken into account. This is the best-fit model for this population when gender, age (calculated in months), marital status, number of people per household, insurance cover, education level, level of physical activity performed each day, diagnosis of diabetes, race/ethnicity, self-reported general health condition, annual income, BMI, and DII are considered. With this multivariate model, the Odds Ratio for DII have similar values to those calculated in the example for the univariate analysis. In this case, when using the same calculation method described in section 4.2.1 of this chapter (using a β value of .0304), the OR calculations yielded the following results: OR= 1.0954, when calculating the difference in odds for chronic pain with a 3-points difference in the DII. OR= 1.3147, when calculating the difference in odds for chronic pain with a 9-points difference in the DII; OR= 1.6265, when calculating the difference in odds for chronic pain with a 16-points difference in the DII.

These results suggest that the relevance of the DII in association with chronic pain in the neck or lower back is affected, but not compromised, by the adjustment to variables relevant in this context.

Table 5. Multivariate analysis of covariates and DII effect on chronic pain presence after manual selection method - final model.

Multivariate analysis: DII on CP (study population) (* = Significant value)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Gender</u>			
	Male		1.00
	Female	p= <.0001*	1.408 (1.226 - 1.618)*
<u>Level of daily physical activity</u>			
	Sit during the day and do not walk about very much		1.00
	Walk a lot during the day, do not carry or lift things very often	p= 0.0208*	0.962 (0.813 - 1.138)
	Lift light load or have to climb stairs or hills often		0.985 (0.794 - 1.221)
	Do heavy work or carry heavy loads		1.472 (1.101 - 1.967)*
<u>Race/Ethnicity</u>			
	Mexican American		0.582 (0.447 - 0.757)*
	Other Hispanic		0.906 (0.636 - 1.291)
	Non-Hispanic White	p= <.0001*	1.00
	Non-Hispanic Black		0.643 (0.512 - 0.808)*
	Other Race – Including Multi-Racial		0.857 (0.624 - 1.176)
<u>General health condition</u>			
	Excellent		1.00
	Very good		1.530 (1.262 - 1.855)*
	Good	p= <.0001*	2.148 (1.763 - 2.616)*
	Fair		3.722 (2.902 - 4.775)*
	Poor		5.846 (3.842 - 8.894)*
<u>Annual Income</u>			
	up to 20.000\$/year		1.00
	20.000 to 45.000\$/year	p= 0.0098*	0.900 (0.733 - 1.105)
	45.000 to 75.000\$/year		0.704 (0.566 - 0.876)*
	over 75.000\$/year		0.834 (0.671 - 1.037)

<u>BMI</u>	p= 0.5196	1.004 (0.993 - 1.015)
<u>DII</u>	p= 0.0430	1.030 (1.001 - 1.061)

4.3 Secondary variable

4.3.1 Univariate analysis

Table 6 below shows the results of analysis performed on the secondary variable of pain lasting more than 24 hours in the month before the interview. This analysis tested for significant association with DII levels, as well as all the covariates that were analyzed with chronic pain in lower back and/or neck. A significant association was found for gender, level of physical activity, diagnosis of diabetes, marital status, race/ethnicity, general health condition, annual income, BMI, and DII. Four variables were found to be non-significantly correlated with pain lasting more than 24 hours: education level, number of people per household, insurance coverage, and age.

The DII was found to be highly significant in the association with pain lasting more than 24 hours ($p < .0001$; OR= 1.073). OR calculations gave the following results using the same calculation method described in section 4.2.1 of this chapter: OR= 1.2355, when calculating the difference in odds for chronic pain with a 3-points difference in the DII; OR= 1.8861, with a 9-points difference in the DII; OR= 3.0895, when calculating the difference in odds for chronic pain with a 16-points difference in the DII.

These results highlight the importance of the DII levels when the presence of pain lasting longer than 24 hours is considered. This association is stronger than that between DII and chronic pain presence in the neck and/or lower back.

Table 6. Univariate analysis of covariates: DII effect on pain lasting more than 24hr in the past month

Univariate analysis: DII on Pain >24hrs (study population n= 3966) (*= Significant value)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Gender</u>			
	Male	p= <.0001*	1.00
	Female		1.394 (1.208 - 1.608)*
<u>Education level</u>			
	Less Than High School	p= 0. 2181	1.00
	High School Diploma		1.030 (0.833 - 1.274)
	More Than High School		0.902 (0.745 - 1.091)
<u>Level of daily physical activity</u>			
	Sit during the day and do not walk about very much	p= 0. 0422*	1.00
	Walk a lot during the day, do not carry or lift things very often		1.247 (0.922 - 1.687)
	Lift light load or have to climb stairs or hills often		1.014 (0.761 - 1.350)
	Do heavy work or carry heavy loads		1.246 (0.908 - 1.708)
<u>Diabetes</u>			
	Yes	p= 0.0006*	1.00
	No		0.614 (0.478 - 0.789)*
	Borderline		0.546 (0.261 - 1.141)
<u>Marital status</u>			
	Married or living with a partner	p= 0. 0211*	1.00
	Widowed, divorced, separated, never married		1.196 (1.027 - 1.392)*

<u>Race/Ethnicity</u>		
Mexican American		0.485 (0.353 - 0.664)*
Other Hispanic		0.826 (0.564 - 1.208)
Non-Hispanic White	p= 0. 0001*	1.00
Non-Hispanic Black		0.800 (0.630 - 1.017)
Other Race – Including Multi-Racial		1.029 (0.742 - 1.428)
<u>Number of people per household</u>		
1		1.00
2		1.032 (0.818 - 1.303)
3	p= 0. 4159	0.943 (0.725 - 1.227)
4		1.173 (0.900 - 1.529)
5+		0.959 (0.734 - 1.253)
<u>Insurance cover</u>		
Yes		1.00
No	p= 0.7058	1.037 (0.858 - 1.254)
<u>General health condition</u>		
Excellent		1.00
Very good		2.133 (1.659 - 2.741)*
Good	p= <.0001*	3.701 (2.906 - 4.714)*
Fair		5.553 (4.225 - 7.297)*
Poor		13.729 (9.208 - 20.471)*
<u>Annual Income</u>		
up to 20.000\$/year		1.00
20.000 to 45.000\$/year		0.828 (0.674 - 1.017)
45.000 to 75.000\$/year	p= <.0001*	0.498 (0.396 - 0.625)*
over 75.000\$/year		0.742 (0.600 - 0.917)*
<u>BMI</u>	p= <.0001*	1.024 (1.013 - 1.035)*
<u>Age (in months)</u>	p= 0.2111	1.000 (1.000 - 1.001)
<u>DII</u>	p= <.0001*	1.073 (1.042 - 1.106)*

4.3.2 Multivariate analysis

When considering DII and the outcome variable of “pain lasting longer than 24 hours”, multivariate analysis (Table 7) was performed including all the variables deemed significant at a .20 level in the univariate analysis, with the results given in Table 7 below. The included variables were gender, education level, level of physical activity performed each day, diagnosis of diabetes, marital status, race/ethnicity, self-reported general health condition, annual income, BMI, and DII.

In this model DII was again found to be highly significant, with a p-value of <.0001. Two covariates lost their significance in this model (diagnosis of diabetes and BMI).

Table 7. Multivariate analysis of covariates and DII effect on pain lasting more than 24hr in the past month – initial model.

Multivariate analysis: DII on Pain >24hrs (study population)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Gender</u>			
	Male	p= <.0001*	1.00
	Female		1.662 (1.416 - 1.951)*
<u>Level of daily physical activity</u>			
	Sit during the day and do not walk about very much	p= 0. 0021*	1.00
	Walk a lot during the day, do not carry or lift things very often		1.021 (0.842 - 1.237)
	Lift light load or have to climb stairs or hills often		1.491 (1.169 – 1.901)*
	Do heavy work or carry heavy loads		1.289 (0.922 - 1.802)

<u>Diabetes</u>			
	Yes		1.00
	No	p= 0.1275	1.097 (0.820 - 1.467)
	Borderline		0.507 (0.227 – 1.134)
<u>Marital status</u>			
	Married or living with a partner		1.00
	Widowed, divorced, separated, never married	p= <.0001*	1.429 (1.197 - 1.705)*
<u>Race/Ethnicity</u>			
	Mexican American		0.348 (0.248 - 0.489)*
	Other Hispanic		0.715 (0.471 - 1.086)
	Non-Hispanic White	p= <. 0001*	1.00
	Non-Hispanic Black		0.639 (0.489 - 0.834)*
	Other Race – Including Multi-Racial		1.124 (0.790 - 1.598)
<u>General health condition</u>			
	Excellent		1.00
	Very good		2.218 (1.709 - 2.878)*
	Good	p= <.0001*	4.201 (3.239 – 5.450)*
	Fair		6.863 (5.076 – 9.279)*
	Poor		19.997(12.760 – 31.277)*
<u>Annual Income</u>			
	up to 20.000\$/year		1.00
	20.000 to 45.000\$/year		0.893 (0.711 - 1.123)
	45.000 to 75.000\$/year	p= <.0001*	0.566 (0.437 - 0.733)*
	over 75.000\$/year		1.033 (0.803 – 1.330)
<u>BMI</u>			
		p= 0.1859	1.008 (0.996 - 1.021)
<u>DII</u>			
		p= <.0001*	1.073 (1.037 - 1.110)*

A stepwise selection method was then performed with all variables included in the multivariate analysis that were found to be significant at least at a .20

p-level. This procedure found that gender, level of physical activity performed each day, marital status, race/ethnicity, self-reported general health condition, annual income, and DII were significant and relevant in defining a statistical model for the analyzed variables. When the multivariate analysis was run again, this time adjusted for these variables (Table 8), DII was highly significant with a p-value of <.0001 and an OR of 1.079. The level of physical activity was significant with a p-value of 0.0021, and all other variables were significant at a <.0001 level. The interactions between these four variables were analyzed by running a separate multivariate analysis for each of the possible interactions between factors, and none were found to be significant.

Table 8. Multivariate analysis of DII effect pain lasting more than 24hr in the past month after manual selection method (Final model).

Final Model: DII on Pain >24hrs (study population)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Gender</u>			
	Male	p= <.0001*	1.00
	Female		1.601 (1.367 - 1.875)*
<u>Level of daily physical activity</u>			
	sit during the day and do not walk about very much	p= 0. 0021*	1.00
	walk a lot during the day, do not carry or lift things very often		0.958 (0.809 - 1.133)
	lift light load or have to climb stairs or hills often		0.973 (0.785 - 1.206)
	do heavy work or carry heavy loads		1.465 (1.097 - 1.957)*
<u>Marital status</u>			
	Married or living with a partner	p= <.0001*	1.00
	Widowed, divorced, separated, never married		1.425 (1.197 - 1.695)*

<u>Race/Ethnicity</u>		
Mexican American		0.571 (0.439 - 0.743)*
Other Hispanic		0.934 (0.655 - 1.333)
Non-Hispanic White	p= <. 0001*	1.00
Non-Hispanic Black		0.675 (0.537 - 0.848)*
Other Race – Including Multi-Racial		0.866 (0.631 - 1.190)
<u>General health condition</u>		
Excellent		1.00
Very good		2.197 (1.700 - 2.841)*
Good	p= <.0001*	4.213 (3.270 – 5.426)*
Fair		6.688 (4.995 – 8.954)*
Poor		17.481(11.416 – 26.770)*
<u>Annual Income</u>		
up to 20.000\$/year		1.00
20.000 to 45.000\$/year	p= <.0001*	0.912 (0.728 - 1.143)
45.000 to 75.000\$/year		0.590 (0.458 - 0.761)*
over 75.000\$/year		1.072 (0.835 – 1.375)
<u>DII</u>	p= <.0001*	1.079 (1.044 – 1.115)*

4.4 Tertiary variable

4.4.1 Univariate analysis

For the population who experienced pain for more than 24 hours, univariate analysis was also performed on the tertiary variable of pain duration, with the results presented in Table 8 below. This variable was dichotomized into pain length longer than 24 hours but shorter than three months and pain length longer than

three months. This analysis found a significant association between pain duration and DII levels (p= 0.0164; OR= 1.012; 95%CI= 1.042 – 1.124).

Table 9. Univariate analysis of covariates: DII effect on pain duration.

Univariate analysis: DII on Pain Duration (study population n= 1033)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Gender</u>			
	Male		1.00
	Female	p= 0.9216	1.012 (0.794 - 1.290)
<u>Education level</u>			
	Less Than High School		1.00
	High School Diploma	p= 0.0004*	0.861 (0.590 - 1.256)
	More Than High School		1.483 (1.061 – 2.072)*
<u>Level of daily physical activity</u>			
	Sit during the day and do not walk about very much		1.00
	Walk a lot during the day, do not carry or lift things very often	p= 0.0002*	1.438 (1.063 – 1.945)*
	Lift light load or have to climb stairs or hills often		1.973 (1.364 – 2.854)*
	Do heavy work or carry heavy loads		2.489 (1.512 – 4.097)*
<u>Diabetes</u>			
	Yes		1.00
	No	p= 0.0816	0.627 (0.407 – 0.965)*
	Borderline		1.074 (0.262 – 4.403)
<u>Marital status</u>			
	Married or living with a partner		1.00
	Widowed, divorced, separated, never married	p= 0.8290	0.971 (0.743 - 1.268)

<u>Race/Ethnicity</u>		
Mexican American		1.573 (0.883 – 2.802)
Other Hispanic		3.262 (1.646 – 6.461)*
Non-Hispanic White	p= 0. 0037*	1.00
Non-Hispanic Black		1.473 (0.972 – 2.234)
Other Race – Including Multi-Racial		1.121 (0.639 - 1.967)
<u>Number of people per household</u>		
1		1.00
2		1.566 (1.015 – 2.416)*
3	p= 0.0045*	1.450 (0.890 - 2.362)
4		2.377 (1.475 – 3.832)*
5+		1.969 (1.209 – 3.206)*
<u>Insurance cover</u>		
Yes		1.00
No	p= 0.1363	0.780 (0.563 - 1.082)
<u>General health condition</u>		
Excellent		1.00
Very good		1.354 (0.864 - 2.122)
Good	p= <.0001*	1.731 (1.127 – 2.659)*
Fair		4.423 (2.709 - 7.220)*
Poor		8.222 (4.126 – 16.385)*
<u>Annual Income</u>		
up to 20.000\$/year		1.00
20.000 to 45.000\$/year		1.546 (1.074 – 2.226)*
45.000 to 75.000\$/year	p= <.0001*	1.200 (0.786 – 1.831)
over 75.000\$/year		2.853 (1.965 – 4.142)*
<u>BMI</u>	p= 0.9486	1.001 (0.983 - 1.019)
<u>Age (in months)</u>	p= <.0001*	0.998 (0.997 – 0.998)*
<u>DII</u>	p= 0.0164*	1.012 (1.042 - 1.124)*

4.4.2 Multivariate analysis

Regarding DII and the outcome variable of pain duration, multivariate analysis was performed including all the variables deemed significant at a .20 level in the univariate analysis. The results of this multivariate analysis are given below in Table 9. Variables included in the analysis were education level, level of physical activity performed each day, race/ethnicity, number of people per household, self-reported general health condition, annual income, age, and DII. The two variables of diagnosis of diabetes and BMI were not included in this analysis.

In this model, the DII was found to be non-significant, with a p-value of 0.2956. Stepwise analysis was not performed since the DII p-value exceeded the previously imposed cut-off point of .20.

Table 10. Multivariate analysis of covariates: DII effect on pain duration.

Multivariate analysis: DII on Pain Duration (study population n= 1033)		Analysis of Maximum Likelihood Estimates	OR and 95% CI
<u>Education level</u>			
	Less Than High School		1.00
	High School Diploma	p= 0.0029*	0.481 (0.313 – 0.741)
	More Than High School		0.691 (0.457 – 1.046)
<u>Level of daily physical activity</u>			
	Sit during the day and do not walk about very much		1.00
	Walk a lot during the day, do not carry or lift things very often	p= 0.1737	1.184 (0.846 – 1.657)
	Lift light load or have to climb stairs or hills often		1.361 (0.903 – 2.051)
	Do heavy work or carry heavy loads		1.827 (1.031 – 3.240)

<u>Race/Ethnicity</u>		
Mexican American		1.573 (0.883 – 2.802)
Other Hispanic		3.262 (1.646 – 6.461)
Non-Hispanic White	p= 0.5839	1.00
Non-Hispanic Black		1.473 (0.972 – 2.234)
Other Race – Including Multi-Racial		1.121 (0.639 - 1.967)
<u>Number of people per household</u>		
1		1.00
2		1.566 (1.015 – 2.416)
3	p= 0.7572	1.450 (0.890 - 2.362)
4		2.377 (1.475 – 3.832)
5+		1.969 (1.209 – 3.206)
<u>General health condition</u>		
Excellent		1.00
Very good		1.483 (0.749 – 2.937)
Good	p= <.0001*	3.485 (1.815 – 6.693)
Fair		4.298 (2.177 – 8.486)
Poor		5.431 (2.550 – 11.567)
<u>Annual Income</u>		
up to 20.000\$/year		1.00
20.000 to 45.000\$/year		1.480 (0.996 – 2.200)
45.000 to 75.000\$/year	p= 0.0005*	0.997 (0.629 – 1.581)
over 75.000\$/year		2.145 (1.370 – 3.358)
<u>Age (in months)</u>	p= 0.0004*	0.998 (0.998 – 0.999)
<u>DII</u>	p= 0.2956	1.033 (0.972 - 1.099)

CHAPTER 5: CONCLUSION

5.1 Discussion.

The results of this study were largely in line with what was anticipated. Due to the lack of previous studies in the literature on the associations between pro-inflammatory diet and chronic pain, no comparison could be made between this study's results and others. Nonetheless, a discussion about these results and their quality, impact and applicability can be found in this chapter.

5.1.1 Baseline characteristics

The baseline characteristics analysis of the population sample highlights some of the major limitations of the current study.

A number of differences were found at baseline for the population >20 years of age (included versus excluded population). Significant differences were found in gender, level of education, level of physical activity performed each day, marital status, race/ethnicity, number of people per household, insurance coverage, annual income, and BMI. These differences made the occurrence of chronic pain more likely within the observed population, therefore limiting the generalizability of the results. Non-significant differences were found for the variables of diagnosis of diabetes, general health conditions and age.

The limitations of the internal validity are highlighted by the numerous differences at baseline for the study population (individuals with chronic pain versus

excluded population). Significant differences were found in gender, level of education, level of physical activity performed each day, diagnosis of diabetes, race/ethnicity, annual income, and BMI. These confounders have an impact on both diet and chronic pain, and their unbalanced presence in this study population have an unpredictable effect. To reduce this effect, all the significantly different confounders from the univariate analysis were adjusted for in the multivariate analysis. All the significant variables in the multivariate analysis were then considered for the selection method used to build the final model.

5.1.2 DII and CP in LB and neck

The univariate analysis performed on the association between DII and relevant covariates and chronic pain presence showed interesting results. DII levels have been found to be significantly associated with the presence of chronic pain in the univariate analysis with a p-value of 0.0099. This p-value is not highly significant, but when examining the OR (1.036) for different levels of DII values (as shown in chapter 4, section 4.2.1), it is clear that a large difference in DII can have a significant impact in the presence of chronic pain.

Although not quite applicable to any real life situation, two diets at the opposite extremes of the DII spectrum would have a highly significant difference in odds (OR=1.7676). These data exemplify the difference that a completely anti-inflammatory diet could have when compared to a fully pro-inflammatory diet. In this extreme example, an individual with a highly pro-inflammatory diet increases the chances of having chronic pain in the lower back or neck by 76.76%, when compared to someone having a completely anti-inflammatory diet. The interpretation of this

result sheds light on the potential importance of diet in relation to chronic pain in lower back and cervical spine. However, these statistics have limited applicability due to the fact that the univariate analysis does not account for confounding effects.

Multivariate analysis of the effect of DII on chronic pain presence showed a loss of significance of the DII itself, when gender, education level, level of physical activity, diagnosis of diabetes, race/ethnicity, general health condition, annual income and BMI were adjusted for in the analysis. Education level, diagnosis of diabetes, and BMI lost significance as well, yet these three factors became strongly non-significant, while DII became non-significant with a p-value of 0.0610. In this analysis, DII, although not significant anymore, may still have some relevance in the construction of the final model, for it still shows an OR that is pointing towards a positive association (OR= 1.028, 95%CI= 0.999 – 1.059). The loss of significance has different possible interpretations, and it may be that the flaws of the population's baseline characteristics taken into account play a role in it. Confounders' distribution may play a significant role in determining the overall effect of the main variable, although it is not possible to draw definite conclusions. It may also be that DII does not have an actual association with the presence of long term pain in lower back and neck.

To make sure that the best model fit all the relevant variables, a stepwise selection method was run with all the factors found to be significant at a p-value of 0.20. The stepwise selection method analysis found that, considering all the significant variables in this analysis, only gender, general health condition, annual income and DII were significant and relevant for the best fitted final model construction.

When a multivariate analysis of the DII effect on chronic pain presence was run again including only the variables found significant in the stepwise selection method, the DII retained significance ($p= 0.0346$), although it was diminished compared to the initially discovered value found in the univariate analysis. The lack of interaction between the variables included in the final model increases the strength of the results found.

When considering this specific population and confounders, DII has a significant, albeit weak, effect on chronic pain in the neck and lower back. This result illustrates the importance of the effect that diet-related inflammation may have on chronic pain. There is a need for more studies in this area to investigate the effect of anti-inflammatory diet on the presence of chronic pain. If results are consistent in future studies, the possibility of an anti-inflammatory diet as a treatment approach should be further investigated as well.

5.1.3 DII and pain > 24 hours

The univariate analysis of covariates and DII effect on pain lasting more than 24 hours in the month prior to the interview also showed significant and interesting results. In this univariate analysis, gender, diagnosis of diabetes, marital status, race/ethnicity, general health condition, annual income, BMI, and DII were all found to be significantly associated with pain lasting more than 24 hours. In contrast, education level, level of physical activity, number of people per household, insurance cover, and age were not found to be significantly associated with the outcome variable. In this case, DII had a very strong significance, with a $p\text{-value} = <.0001$, $OR = 1.073$, and $95\%CI = 1.042 - 1.106$. This result points to the possibility that

inflammation may be an important predisposing factor for chronic pain. If individuals with higher diet-related inflammation levels are more likely to have pain for longer than 24 hours, then it is possible that this inflammation plays a role as one of the early predisposing factors for the development of chronic pain.

The multivariate analysis of the effect that DI has on pain lasting more than 24 hours in the preceding month was also performed with all the significant covariates accounted for in the model. The DII retained its significance and neither its p-value, nor its OR changed. Diabetes and BMI lost their significance, although with a p-value lower than 0.2, and were therefore included in the stepwise selection method. The selection method confirmed that both factors were non-significant in this model, together with age, while all of other confounders proved significant. The DII maintained its significance and its OR increased to 1.079 (95%CI of 1.044 to 1.115) when non-significant variables were taken out of the final model. No interactions were found to be significant between the variables included in the final model.

A strong association is therefore evidenced between DII levels and pain lasting longer than 24 hours. This association made the further analysis of pain duration more relevant.

5.1.4 DII and pain duration

The last analysis performed for this study involved the univariate analysis of DII and relevant covariates on pain duration, dichotomized as pain less than three months and pain longer than three months. An analysis of each of the variables found education level, level of physical activity, race/ethnicity, number of people per household, general health condition, annual income, age, and DII to be all

significantly associated with pain lasting more than three months. Gender, diagnosis of diabetes, marital status, insurance cover, and BMI were all found to be non-significantly associated with the outcome variable. In this case, DII was significant, with a p-value= 0.00164, OR= 1.012, and 95%CI= 1.042 to 1.106.

Multivariate analysis of the DII's effect on pain duration was then performed with all significant covariates accounted for in the model. DII lost its significance with a p-value= 0.2956 and an OR= 1.033 and 95%CI= (0.972 - 1.099). This significance-value was above the threshold of the $p= 0.20$ that was applied for the other stepwise analyses. For this reason, the stepwise calculation method was not performed for this model. Lack of control for the confounders might have played a prominent role in the loss of significance found in the univariate analysis. Considering the weaknesses of this study, as well as the significant level found in the univariate analysis, it is reasonable that a better study design would yield more conclusive results. Therefore, further investigations on this topic are needed.

Nonetheless, from these results it seems that diet-related inflammation levels might be minimally involved with a duration of pain longer than three months.

5.1.5 Interpreting the DII

To interpret the results from this study, it is important to have an understanding of how to match DII scores to specific diets. A variety of factors play a role in the final DII score, and it is therefore important to understand these factors and how they are related to different foods and diets. When considering the 45 items used for the calculation of the DII, only 9 items have pro-inflammatory effects, while the remaining 36 have a protective effect towards inflammation. It is therefore important

to understand why the majority of people assessed in this study tended towards a pro-inflammatory diet.

First, the quantities consumed of each of these food components must be considered. While the number of food items that are anti-inflammatory is higher than the pro-inflammatory ones, pro-inflammatory food components are mainly macronutrients (e.g., carbohydrate, total fat, cholesterol, protein, saturated fats, trans fats and total energy intake calculated in kcal). For this reason, they are consumed in much higher quantities than the anti-inflammatory food components, which are mainly micronutrients (e.g., vitamins, oligo minerals, flavonoids), spices (e.g., garlic, ginger, saffron, turmeric, pepper, thyme and rosemary), higher-quality fats (e.g., MUFA, PUFA, n-3 fatty acids, and n-6 fatty acids), and dietary fibers. These food components are mostly present in items that do not play a major role in the typical diet adopted in most western countries. Keeping in mind that the calculation of DII score depends on the inflammatory effect score applied to the effective quantities of food eaten, higher quantities of foods consumed will have a stronger effect on the final score calculation.

Second, the way that combinations of foods in different diets impact the final DII score must be considered. In order to understand how different diets impact the DII, it is important to understand how the 45 food components are represented in foods of general consumptions. In order to give real-life examples, two typical dietary patterns (described in chapter 3) are analyzed: the “Western dietary pattern” (WDP), which has been associated with a pro-inflammatory effect, and the “prudent dietary pattern” (PDP) which has been associated with an anti-inflammatory effect.

In the WDP, there is a preponderance in the consumption of meats (both red and processed), butter and other high-fat dairy products, eggs, white potatoes, refined grains, high-sugar drinks and processed food containing elevated quantities of refined sugars and hydrogenated oils. This diet is severely skewed towards the consumption of pro-inflammatory food components, such as carbohydrates and total energy intake (due to the elevated amounts of refined sugars as well as refined grains), proteins, cholesterol, and total fat intake (due to the elevated amounts of animal products such as meats dairies and eggs), and higher trans fats intake (due to the elevated amounts of processed foods)^[294]. On the other hand, in the PDP, the consumption of most of the anti-inflammatory items is heightened as a result of the increased consumption of fruits and vegetables (major source of vitamins, flavonoids and oligo minerals), mono-unsaturated fat sources (such as olive oil), poly-unsaturated fat sources (e.g. nuts and fish), and whole grains (important source of dietary fibers). The lower consumption of processed food leaves more space for cooking, which usually involves a higher use of spices and herbs. Additionally, a diet that has a higher proportion of fruits and vegetables consumption in contrast to higher consumption of meats, refined sugars and processed foods typically results in lower overall caloric intake, which is relevant for the DII calculation as well.

5.1.6 Overall considerations

The results from this study highlight the association of diet-related inflammation (analyzed through the calculation of the DII score) with chronic pain. The overall conclusions drawn from these analyses open up a promising perspective for a better understanding of chronic pain mechanisms. It is already widely known

that chronic pain is multifactorial ^[295-297]. It appears from the results of this study that diet-related inflammation may be considered as one of these contributing factors. Specifically, the data point towards an association between DII levels and presence of chronic pain in the neck and lower back, as well as towards a very strong association between DII levels and pain lasting more than 24 hours. It appears, therefore, that DII levels might be participating in the process of predisposing for chronic pain, by making the recovery from the initial pain longer. It also seems that DII levels might be a relevant factor involved in determining the length of pain; however, it may not be the main factor, as DII scores showed a weak association with pain lasting longer than three months. This association points to a possible direct link between DII levels and chronic pain, which should be further investigated.

No other studies could be found that addressed the association between diet-related inflammation (measured with DII) and presence of chronic pain, and promising results have been highlighted. There is a need for further studies in this area with a more sensible study design. These further studies should be tailored to the specific characteristics of the chronic pain population. For example, there have been studies that showed the importance of sub-classification in the treatment of both sub-acute and chronic pain population ^[298, 299]. The ability to provide a specific therapeutic approach for different sub-groups within the chronic pain population has proven to heighten response to treatment. Therefore, it should be kept in mind that the chronic pain population can have very different combinations of contributing factors to the origin and perpetration of pain. Diet-related inflammation may be more relevant to a specific sub-group within the general chronic pain population than other, less affected

sub-groups. Sub-classification should be considered when designing or analyzing the results of studies on chronic pain.

5.2 Limitations

The dataset used was the only one found that included all the data necessary for calculating DII and the data regarding non-arthritic and idiopathic pain. Since the dataset is from 2003-2004, it might not be a valid representation of the current US population (in 2017). Additionally, generalizing the conclusions to any other country may be of limited value. Nonetheless, the large number of individuals included in the study counterbalances, at least in part, this limitation.

A second limitation is that both the internal and external validity were decreased in this study, making the overall generalizability of the results fairly weak. A large dataset was used, meant that the results could be potentially significant and relevant. However, when considering the results of the Pearson's χ^2 test and t-test for baseline characteristics though, many differences were highlighted at baseline. Differences were found for both the target population and the study population.

The analysis of the baseline characteristics of the included population versus the excluded (> 20yrs old) highlights a limited generalizability (external validity) of the study results. Among the 12 known confounding factors for chronic pain populations analyzed, eight were found to be significantly different in this study.

Another limitation of this study arises from the results of the analysis of baseline characteristics of the study population (included population: chronic pain vs.

non-chronic pain presence). When comparing baseline characteristics of individuals with chronic pain versus individuals without chronic pain, significant differences were found. Among the 12 known confounding factors for chronic pain populations that were analyzed, eight were found to be significantly different in this study. These differences highlight limited internal validity for the study results. The chronic pain population had a higher percentage of female, a higher percentage of high school diploma or more than high school diploma, a higher percentage of people doing very little physical activity or heavy duty jobs, a higher percentage of diagnosed diabetes, a higher percentage of self-reported good, fair, and poor health status (versus excellent and very good status), a higher incidence of income under 45,000USD/year and a higher, although minimally so, BMI. These results are consistent with the cofounders associated with chronic pain that could be found in current literature. On the other hand, in regards to the race/ethnicity significant differences, the population with chronic pain shows a higher percentage of non-Hispanic whites and African-Americans, which goes against the current evidence of being white as having a protective effect towards chronic pain ^[274, 300]. The mechanisms behind this difference in perceiving the pain experience are yet to be understood ^[301].

Having these eight above-mentioned confounders balanced between the two groups (chronic pain vs. non-chronic pain presence) would have made the results of this study stronger and more generalizable. These confounders were adjusted for in the multivariate model, which helped increase the internal validity, but questions can still be raised about its strength. Further studies involving dietary changes in a chronic pain population should aim at reducing the presence of confounders in the study population.

The third main weakness of this study is that the information about pain, although still applicable to the physiotherapy field, could have been defined more clearly. This is especially true for the main variable definition, which is lacking a clear description of the amount of time that an individual experienced pain for during the three months preceding the study. The definition of pain in the relevant questions regarding lower back and neck is “pain that lasted a whole day or more”. It is specified that only major pains were to be reported, disregarding any “aches and pains that were fleeting or minor”. The definition used leaves the possibility of misinterpretation by patients and decreases the strength of the results.

Furthermore, the data collected does not follow the most updated definition of chronic pain (which was updated in 2012). This would need to be addressed in future data collection for improving generalizability and relevance to the pain medicine field. Moreover, relevant information for the pain medication used by patients is lacking and should be considered for further investigations. Other data points that should be collected include pain levels, pain impact on physical function, and ADL (activity of daily living) level.

A fourth limitation is that the dietary information was collected solely from the 24-hour recall questionnaire. Even though the questionnaire has been validated and is a reliable tool for data collection of dietary consumption, it has limitations in detecting the full spectrum of variability of an individual’s food consumption. The data collection comes from a patient’s recall, which is always subject to biases, and the recall period is limited to the 24 hours prior to questionnaire completion. The fact that the variables used in this study for conducting the analysis

were averaged between two days' random collection of such data helps with reducing this problem, but does not solve it. A dataset with a wider time range for collecting dietary information could be used in future studies (e.g., the Food Frequency Questionnaire).

Lastly, considering only DII and a limited set of covariates and confounding variables in relation to chronic pain is a limitation as well. Many other factors may be involved in the experience of chronic pain that were outside the scope of this study or could not be assessed using this dataset.

5.3 Implications

5.3.1 Diet and pain

Both diet and pain are major components of human life, and yet the current evidence on the interaction between them is still lacking. In many cases, there is not enough information to support evidenced-based decisions in regards to which diet would better suit an individual's needs. Researchers are starting to look at the relationships between diet and chronic conditions with increasing attention and with a broader approach. Already, many chronic illnesses (the majority of conditions affecting our society) have been associated with specific dietary patterns or consumption of specific foods, according to Vos et al.^[302]. It is suggested from this study that chronic pain, being a systemic condition mediated by different pathways in the body, could also be mediated by inflammation.

5.3.2 Diet assessment as an outcome predictor tool

Another potential implication involves the development of a specific diet-related inflammation questionnaire about dietary habits. This questionnaire could be used during the intake of chronic pain patients, as well as during the intake of new acute patients to possibly predict the development of chronic pain. The development of such a questionnaire is a challenge, as multiple factors need to be taken into consideration. Dietary assessments present challenges coming from individual changes in diet, variability of the food consumed, and presence of processed foods (which usually have complex ingredients lists).

There is a need for research addressing the relationship between chronic pain and dietary pattern to define and investigate the relevant clinical sub-groups so that they could be properly addressed.

5.3.3 Diet change as possible pain treatment

Pain mechanisms underlying chronicity are complex, just as much as diet effects on the human body are. Therefore, the association found between these two factors helps with the understanding of both. The present study points at a new possible approach to the multi-dimensional understanding of the chronicity of pain.

The implications of this understanding extend into possible future ways of treating CP. For example, a new approach could involve referring these patients to a professional dietician. This professional can address the dietary issues by adjusting the patient's diet and reduce the systemic inflammatory effects mediated by the patient's current food intake.

5.4 Conclusion

This study examined the association between diet-related inflammation, measured with DII, and the presence of neck and lower back pain in the three months before the interview. Presence of pain for at least three months falls into the definition of chronic pain, a highly prevalent condition in the general population of Western countries, which results in high direct and indirect costs. The presence of pain in neck and lower back was found to be associated with DII levels. More specifically, higher levels of DII, a result of a pro-inflammatory diet, were associated with higher odds of pain presence in neck and lower back.

The study also analyzed the levels of DII in relation to pain lasting for longer than 24 hours. This step was taken to further understand the time dependent association between DII and CP. Presence of pain for a period longer than 24 hours was found to be significantly associated with DII levels. More specifically, higher levels of DII were associated with higher odds of pain presence for a period lasting longer than 24 hours.

People who self-reported having pain for longer than 24 hours were then asked the duration they had pain for, which was the third variable studied. Those individuals were screened by analyzing the association between DII levels and pain duration. This variable was dichotomized as pain lasting less than three months and pain lasting longer than three months. Although the latter analysis (dichotomized pain duration) was performed on a smaller population (n= 1033) compared to the population (n= 3966) analyzed for the main variable and the secondary variable, it still provided interesting results. Pain lasting longer than 24 hours, as well as pain

lasting longer than three months, was found to be associated with higher levels of DII. While the former showed a strong significance level that retained its significance in the final model, the latter showed a weaker significant association which lost its significance in the multivariate analysis. The results show that the DII levels do not have a significant association with pain duration when this variable is dichotomized with a three-month cut-off point. It may be that the loss in significance could be related to a different size of population taken into account for the statistical analysis, as well as to the difference in baseline characteristics for that population. Further studies may help understand further.

Overall, this study provided interesting results in addressing the research question on diet-related inflammation associated with chronic pain. Furthermore, it appears that the level of diet-related inflammation calculated with the DII plays a role in the etiology mechanism of chronic pain and possibly in its perpetration. More research is required in this area to better understand the involved mechanisms.

5.5 Ethical considerations.

According to the current literature, no risks were anticipated nor foreseen in regards of physical, emotional or psychosocial harm. Datasets do not contain any identifiers. The HREA, the ethics committee board for the province of Newfoundland and Labrador, cleared the study from the need of seeking ethics approval. The dataset was downloaded from the CDC website ^[68] and kept on the PI's computer.

According to the definition of the study population, no participants requiring additional consideration were included. Considering the use of secondary

data, which does not involve any intervention and does not anticipate any risk, there was no need for any special consideration, other than the ones already considered.

At the time of data collection from the NHANES, ethics approval was sought from the NCHS Research Ethics Review Board (ERB) and granted. Consent was obtained from each participant, in the case of interview only, or twice in the event of both an interview and examination.

No conflicts of interest are present.

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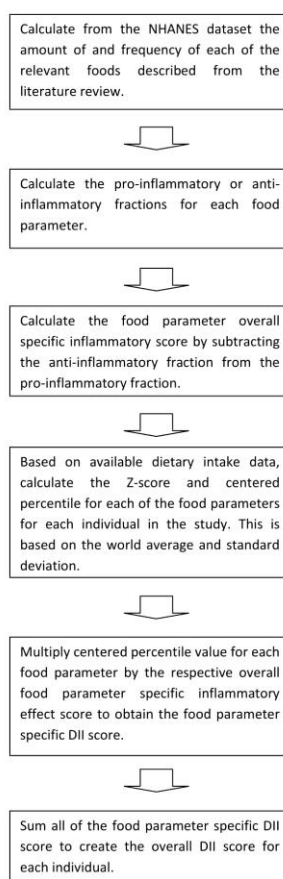
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APPENDIX

Appendix 1.

DII calculation flowchart



Appendix 2.

NHANES Food Questionnaire

***More than one member of your household
may have received a questionnaire.
Please make sure this is your booklet
before answering any questions.***



LABEL HERE

GENERAL INSTRUCTIONS

- Answer each question as best you can. Estimate if you are not sure. A guess is better than leaving a blank.
- Use only a No. 2 pencil.
- Be certain to completely blacken in each of the answers.
- Erase completely if you make any changes.
- Do not make any stray marks on this form.
- If you blacken NEVER or NO for a question, please follow any arrows or instructions that direct you to the next question.

PLEASE DO NOT WRITE IN THIS AREA

[illegible]

SERIAL #

Public reporting burden of this collection of information is estimated to be 45 minutes per response for total participation, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. An agency may not conduct or sponsor, and a person is not required to respond to collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspects of this collection of information, including suggestions for reducing burden to: CDC/ATSDR Reports Clearance Officer, 1800 Clifton Road, MS D-24, Atlanta, GA 30333, Attention: PRA (0920-0237).

1. Over the past 12 months, how often did you drink **tomato juice** or **vegetable juice**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 2–3 times per day |
| <input type="radio"/> 1–2 times per week | <input type="radio"/> 4–5 times per day |
| <input type="radio"/> 3–4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5–6 times per week | |

2. How often did you drink **orange juice** or **grapefruit juice**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 2–3 times per day |
| <input type="radio"/> 1–2 times per week | <input type="radio"/> 4–5 times per day |
| <input type="radio"/> 3–4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5–6 times per week | |

3. How often did you drink **apple juice**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 2–3 times per day |
| <input type="radio"/> 1–2 times per week | <input type="radio"/> 4–5 times per day |
| <input type="radio"/> 3–4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5–6 times per week | |

4. How often did you drink **grape juice**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 2–3 times per day |
| <input type="radio"/> 1–2 times per week | <input type="radio"/> 4–5 times per day |
| <input type="radio"/> 3–4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5–6 times per week | |

5. How often did you drink **other 100% fruit juice** or **100% fruit juice mixtures** (such as pineapple, prune, or others)?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 2–3 times per day |
| <input type="radio"/> 1–2 times per week | <input type="radio"/> 4–5 times per day |
| <input type="radio"/> 3–4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5–6 times per week | |

6. How often did you drink other **fruit drinks** (such as cranberry cocktail, Hi-C, lemonade, or Kool-Aid, diet or regular)?

☐ NEVER (GO TO QUESTION 7)

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 2–3 times per day |
| <input type="radio"/> 1–2 times per week | <input type="radio"/> 4–5 times per day |
| <input type="radio"/> 3–4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5–6 times per week | |

- 6a. How often were your fruit drinks **diet** or **sugar-free drinks**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

7. How often did you drink **milk as a beverage** (NOT in coffee, NOT in cereal)? (Please include chocolate milk and hot chocolate.)

☐ NEVER (GO TO QUESTION 8)

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 2–3 times per day |
| <input type="radio"/> 1–2 times per week | <input type="radio"/> 4–5 times per day |
| <input type="radio"/> 3–4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5–6 times per week | |

- 7a. What kind of **milk** did you usually drink?

- ☐ Whole milk
☐ 2% fat milk
☐ 1% fat milk
☐ Skim, nonfat, or 1/2% fat milk
☐ Soy milk
☐ Rice milk
☐ Raw, unpasteurized milk
☐ Other

BAR

CODE

LABEL

HERE



Question 8 appears on the next page.

Over the past 12 months...

8. How often did you drink **meal replacement, energy, or high-protein beverages** such as Instant Breakfast, Ensure, Slimfast, Sustacal or others?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 1-2 times per week | <input type="radio"/> 4-5 times per day |
| <input type="radio"/> 3-4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5-6 times per week | |

9. Over the past 12 months, did you drink **soft drinks, soda, or pop**?

☐ NO (GO TO QUESTION 10)

☐ YES

9a. How often did you drink **soft drinks, soda, or pop IN THE SUMMER**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 1-2 times per week | <input type="radio"/> 4-5 times per day |
| <input type="radio"/> 3-4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5-6 times per week | |

9b. How often did you drink **soft drinks, soda, or pop DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 1-2 times per week | <input type="radio"/> 4-5 times per day |
| <input type="radio"/> 3-4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5-6 times per week | |

9c. How often were these soft drinks, soda, or pop **diet or sugar-free**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

9d. How often were these soft drinks, soda, or pop **caffeine-free**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

Question 10 appears in the next column.

10. Over the past 12 months, did you drink **beer**?

☐ NO (GO TO QUESTION 11)

☐ YES

10a. How often did you drink **beer IN THE SUMMER**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 1-2 times per week | <input type="radio"/> 4-5 times per day |
| <input type="radio"/> 3-4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5-6 times per week | |

10b. How often did you drink **beer DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 1-2 times per week | <input type="radio"/> 4-5 times per day |
| <input type="radio"/> 3-4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5-6 times per week | |

11. How often did you drink **wine or wine coolers**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 1-2 times per week | <input type="radio"/> 4-5 times per day |
| <input type="radio"/> 3-4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5-6 times per week | |

12. How often did you drink **liquor or mixed drinks**?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> 1 time per month or less | <input type="radio"/> 1 time per day |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 1-2 times per week | <input type="radio"/> 4-5 times per day |
| <input type="radio"/> 3-4 times per week | <input type="radio"/> 6 or more times per day |
| <input type="radio"/> 5-6 times per week | |



Over the past 12 months...

13. Did you eat **oatmeal, grits, or other cooked cereal**?

☐ NO (GO TO QUESTION 14)

☐ YES

13a. How often did you eat **oatmeal, grits, or other cooked cereal IN THE WINTER**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per winter | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per winter | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

13b. How often did you eat **oatmeal, grits, or other cooked cereal DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

13c. How often was the cooked cereal you ate **oatmeal**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

14. How often did you eat **cold cereal**?

☐ NEVER (GO TO QUESTION 15)

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |



Question 15 appears in the next column.

14a. How often was the cold cereal you ate a **whole grain type** (such as shredded wheat, Wheaties, Cheerios, Raisin Bran or other bran, oat, or whole wheat cereal)?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

14b. Was **milk** added to your cold cereal?

☐ NO (GO TO QUESTION 15)

☐ YES

14c. What kind of **milk** was usually added?

- ☐ Whole milk
☐ 2% fat milk
☐ 1% fat milk
☐ Skim, nonfat, or 1/2% fat milk
☐ Soy milk
☐ Rice milk
☐ Raw, unpasteurized milk
☐ Other

15. How often did you eat **applesauce**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

16. How often did you eat **apples**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

17. How often did you eat **pears** (fresh, canned, or frozen)?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Over the past 12 months...

18. How often did you eat **bananas** ?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

19. How often did you eat **pineapple**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

20. How often did you eat **dried fruit**, such as prunes or raisins?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

21. Over the past 12 months, did you eat **peaches, nectarines, or plums**?

☐ NO (GO TO QUESTION 22)

☐ YES

21a. How often did you eat **fresh peaches, nectarines, or plums WHEN IN SEASON**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per season | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |



Question 22 appears in the next column.

21b. How often did you eat **peaches, nectarines, or plums** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

22. How often did you eat **grapes**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

23. Over the past 12 months, did you eat **melons** (such as cantaloupe, watermelon, or honeydew)?

☐ NO (GO TO QUESTION 24)

☐ YES

23a. How often did you eat **fresh melons** (such as cantaloupe, watermelon, or honeydew) **WHEN IN SEASON**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per season | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

23b. How often did you eat **fresh or frozen melons** (such as cantaloupe, watermelon, or honeydew) **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Question 24 appears on the next page.

Over the past 12 months...

24. Did you eat **strawberries**?

☐ NO (GO TO QUESTION 25)

☐ YES

24a. How often did you eat **fresh strawberries WHEN IN SEASON?**

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per season | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

24b. How often did you eat **fresh or frozen strawberries DURING THE REST OF THE YEAR?**

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

25. Over the past 12 months, did you eat **oranges, tangerines, clementines, or tangelos**?

☐ NO (GO TO QUESTION 26)

☐ YES

25a. How often did you eat **fresh oranges, tangerines, clementines, or tangelos WHEN IN SEASON?**

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per season | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Question 26 appears in the next column.

25b. How often did you eat **oranges, tangerines, clementines, or tangelos** (fresh or canned) **DURING THE REST OF THE YEAR?**

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

26. Over the past 12 months, did you eat **grapefruit**?

☐ NO (GO TO QUESTION 27)

☐ YES

26a. How often did you eat **fresh grapefruit WHEN IN SEASON?**

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per season | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

26b. How often did you eat **grapefruit** (fresh or canned) **DURING THE REST OF THE YEAR?**

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

27. How often did you eat **other kinds of fruit**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |



Over the past 12 months...

28. How often did you eat **COOKED greens** (such as spinach, turnip, collard, mustard, chard, or kale)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

29. How often did you eat **RAW greens** (such as spinach, turnip, collard, mustard, chard, or kale)?
(We will ask about lettuce later.)

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

30. How often did you eat **coleslaw**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

31. How often did you eat **sauerkraut or cabbage** (other than coleslaw)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

32. How often did you eat **carrots** (fresh, canned, or frozen)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

33. How often did you eat **string beans or green beans** (fresh, canned, or frozen)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

34. How often did you eat **peas** (fresh, canned, or frozen)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

35. Over the past 12 months, did you eat **corn**?

☐ NO (GO TO QUESTION 36)

☐ YES

35a. How often did you eat **corn** (fresh, canned, or frozen) **WHEN IN SEASON**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per season | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

35b. How often did you eat **corn** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |



Question 36 appears on the next page.

Over the past 12 months...

36. How often did you eat **broccoli** (fresh or frozen)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

37. How often did you eat **cauliflower** or **Brussels sprouts** (fresh or frozen)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

38. How often did you eat **mixed vegetables**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

39. How often did you eat **onions** (including in mixtures)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

40. Over the past 12 months, how often did you eat **sweet or hot peppers** (green, red, or yellow)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

41. How often did you eat **raw cucumbers** (not including pickles)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

42. Over the past 12 months, did you eat **fresh tomatoes** (including those in salads)?

☐ NO (GO TO QUESTION 43)

☐ YES

42a. How often did you eat **fresh tomatoes** (including those in salads) **WHEN IN SEASON**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per season | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

42b. How often did you eat **fresh tomatoes** (including those in salads) **DURING THE REST OF THE YEAR**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |



Question 43 appears on the next page.

Over the past 12 months...

43. Did you eat **summer squash** (include yellow and green squash)?

☐ NO (GO TO QUESTION 44)

☐ YES

43a. How often did you eat **summer squash WHEN IN SEASON** (include yellow and green squash)?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per season | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per season | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

43b. How often did you eat **summer squash DURING THE REST OF THE YEAR** (include yellow and green squash)?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

44. How often did you eat **lettuce salads** (with or without other vegetables)?

☐ NEVER (GO TO QUESTION 45)

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

44a. How often were the lettuce salads you ate made with **dark green leaves**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always



Question 45 appears in the next column.

45. How often did you eat **salad dressing** (including low-fat) on salads or other vegetables?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

46. How often did you eat **sweet potatoes or yams**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

47. How often did you eat **French fries, home fries, hash browned potatoes, or tater tots**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

48. How often did you eat **potato salad**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

49. How often did you eat **baked, boiled, or mashed potatoes**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Over the past 12 months...

50. How often did you eat **salsa**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

51. How often did you eat **catsup**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

52. How often did you eat **pickles or pickled vegetables**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

53. How often did you eat **stuffing, dressing, or dumplings**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

54. How often did you eat **chili**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

55. How often did you eat **tortillas or tacos**?

- ☐ NEVER (GO TO QUESTION 56)
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

55a. How often were your tortillas or tacos **corn tortillas or tacos**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

56. How often did you eat **cooked dried beans** (such as baked beans, pintos, kidney, blackeyed peas, lima, lentils, soybeans, or refried beans)? (Please don't include bean soups or chili.)

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

57. How often did you eat **other kinds of vegetables**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

58. How often did you eat **rice or other cooked grains** (such as bulgur, cracked wheat, or millet)?

- ☐ NEVER (GO TO QUESTION 59)
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Question 59 appears on the next page.

Over the past 12 months...

58a. How often was the rice or other cooked grains you ate **brown rice, cracked wheat, or millet**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

59. How often did you eat **pancakes, waffles, or French toast**?

☐ NEVER (GO TO QUESTION 60)

- ☐ 1-6 times per year ☐ 2 times per week
☐ 7-11 times per year ☐ 3-4 times per week
☐ 1 time per month ☐ 5-6 times per week
☐ 2-3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

59a. How often was **syrup** added to your pancakes, waffles, or French toast?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

60. How often did you eat **lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini**? (Please do not include spaghetti or other pasta.)

☐ NEVER

- ☐ 1-6 times per year ☐ 2 times per week
☐ 7-11 times per year ☐ 3-4 times per week
☐ 1 time per month ☐ 5-6 times per week
☐ 2-3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

61. How often did you eat **macaroni and cheese**?

☐ NEVER

- ☐ 1-6 times per year ☐ 2 times per week
☐ 7-11 times per year ☐ 3-4 times per week
☐ 1 time per month ☐ 5-6 times per week
☐ 2-3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

62. How often did you eat **pasta salad or macaroni salad**?

☐ NEVER

- ☐ 1-6 times per year ☐ 2 times per week
☐ 7-11 times per year ☐ 3-4 times per week
☐ 1 time per month ☐ 5-6 times per week
☐ 2-3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

63. Other than the pastas listed in Questions 60, 61, and 62, how often did you eat **pasta, spaghetti, or other noodles**?

☐ NEVER (GO TO QUESTION 64)

- ☐ 1-6 times per year ☐ 2 times per week
☐ 7-11 times per year ☐ 3-4 times per week
☐ 1 time per month ☐ 5-6 times per week
☐ 2-3 times per month ☐ 1 time per day
☐ 1 time per week ☐ 2 or more times per day

63a. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce or spaghetti sauce made WITH meat**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

63b. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce or spaghetti sauce made WITHOUT meat**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

63c. How often did you eat your pasta, spaghetti, or other noodles with **margarine, butter, oil, or cream sauce**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always



Question 64 appears on the next page.

Over the past 12 months...

64. How often did you eat **bagels** or **English muffins**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

The next questions ask about your intake of breads other than bagels or English muffins. First, we will ask about bread you ate as part of sandwiches only. Then we will ask about all other bread you ate.

65. How often did you eat **breads** or **rolls AS PART OF SANDWICHES** (including burger and hot dog rolls)?

- ☐ NEVER (GO TO QUESTION 66)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

65a. How often were the breads or rolls that you used for your sandwiches **white bread** (including burger and hot dog rolls)?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

66. How often did you eat **breads** or **dinner rolls, NOT AS PART OF SANDWICHES**?

- ☐ NEVER (GO TO QUESTION 67)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

66a. How often were the breads or rolls you ate **white bread**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

Question 67 appears in the next column.

67. How often did you eat **jam, jelly, or honey** on bagels, muffins, bread, rolls, or crackers?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

68. How often did you eat **peanut butter** or **other nut butter**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

69. How often did you eat **roast beef** or **steak IN SANDWICHES**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

70. How often did you eat **turkey** or **chicken COLD CUTS** (such as loaf, luncheon meat, turkey ham, turkey salami, or turkey pastrami)? (We will ask about other turkey or chicken later.)

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

71. How often did you eat **luncheon** or **deli-style ham**? (We will ask about other ham later.)

- ☐ NEVER (GO TO QUESTION 72)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Question 72 appears on the next page.

Over the past 12 months...

71a. How often was the luncheon or deli-style ham you ate **light, low-fat, or fat-free**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

72. How often did you eat **other cold cuts or luncheon meats** (such as bologna, salami, corned beef, pastrami, or others, including low-fat)? *(Please do not include ham, turkey, or chicken cold cuts.)*

☐ NEVER (GO TO QUESTION 73)

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

72a. How often were the other cold cuts or luncheon meats you ate **light, low-fat, or fat-free**? *(Please do not include ham, turkey, or chicken cold cuts.)*

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

73. How often did you eat **canned tuna** (including in salads, sandwiches, or casseroles)?

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

74. How often did you eat **GROUND chicken or turkey**? *(We will ask about other chicken and turkey later.)*

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

75. How often did you eat **beef hamburgers or cheeseburgers**?

☐ NEVER (GO TO QUESTION 76)

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

75a. How often were the beef hamburgers or cheeseburgers you ate made with **lean ground beef**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

76. How often did you eat **ground beef in mixtures** (such as meatballs, casseroles, chili, or meatloaf)?

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

77. How often did you eat **hot dogs or frankfurters**? *(Please do not include sausages or vegetarian hot dogs.)*

☐ NEVER (GO TO QUESTION 78)

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

77a. How often were the hot dogs or frankfurters you ate **light or low-fat hot dogs**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always



Question 78 appears on the next page.

Over the past 12 months...

78. How often did you eat beef mixtures such as **beef stew, beef pot pie, beef and noodles, or beef and vegetables**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

79. How often did you eat **roast beef or pot roast**?
(Please do not include roast beef or pot roast in sandwiches.)

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

80. How often did you eat **steak** (beef)? (Do not include steak in sandwiches)

☐ NEVER (GO TO QUESTION 81)

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

- 80a. How often was the steak you ate **lean steak**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

81. How often did you eat **pork or beef spareribs**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |



82. How often did you eat **roast turkey, turkey cutlets, or turkey nuggets** (including in sandwiches)?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

83. How often did you eat **chicken** as part of **salads, sandwiches, casseroles, stews, or other mixtures**?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

84. How often did you eat **baked, broiled, roasted, stewed, or fried chicken** (including nuggets)?
(Please do not include chicken in mixtures.)

☐ NEVER (GO TO QUESTION 85)

- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

- 84a. How often was the chicken you ate **fried chicken** (including deep fried) or **chicken nuggets**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

- 84b. How often was the chicken you ate **WHITE meat**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

Question 85 appears on the next page.

Over the past 12 months...

84c. How often did you eat chicken **WITH skin**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

85. How often did you eat **baked ham** or **ham steak**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

86. How often did you eat **pork** (including chops, roasts, and in mixed dishes)? *(Please do not include ham, ham steak, or sausage.)*

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

87. How often did you eat **gravy** on meat, chicken, potatoes, rice, etc.?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

88. How often did you eat **liver** (all kinds) or **liverwurst**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

89. How often did you eat **bacon** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 90)
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

89a. How often was the bacon you ate **light, low-fat, or lean bacon**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

90. How often did you eat **sausage** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 91)
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

90a. How often was the sausage you ate **light, low-fat, or lean sausage**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

91. How often did you eat **smoked fish** or **seafood** (such as smoked salmon, lox, or others)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

92. How often did you eat **sushi**?

- ☐ NEVER (GO TO QUESTION 93)
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Question 93 appears on the next page.

Over the past 12 months...

92a. How often did the **sushi** you ate contain **raw fish or seafood** (including shellfish)?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

93. How often did you eat **raw oysters, raw clams, or other raw fish** (not including raw fish in sushi)?

- ☐ NEVER
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

94. How often did you eat **fish sticks or fried fish** (including fried seafood or shellfish)?

- ☐ NEVER
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

95. How often did you eat **all other fish or seafood** (including shellfish) that was **NOT FRIED, SMOKED, or RAW**?

- ☐ NEVER
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

96. How often did you eat **tofu, soy burgers, or soy meat-substitutes**?

- ☐ NEVER
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

97. Over the past 12 months, did you eat **soups**?

☐ NO (GO TO QUESTION 98)

☐ YES

97a. How often did you eat **soup DURING THE WINTER**?

- ☐ NEVER
- ☐ 1–6 times per winter
- ☐ 7–11 times per winter
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

97b. How often did you eat **soup DURING THE REST OF THE YEAR**?

- ☐ NEVER
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

97c. How often were the soups you ate **bean soups**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

97d. How often were the soups you ate **cream soups** (including chowders)?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

97e. How often were the soups you ate **tomato or vegetable soups**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always



Question 98 appears on the next page.

Over the past 12 months...

97f. How often were the soups you ate **broth soups** (including chicken) **with** or **without** noodles or rice?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

98. How often did you eat **pizza**?

☐ NEVER (GO TO QUESTION 99)

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

98a. How often did you eat pizza with **pepperoni**, **sausage**, or **other meat**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

99. How often did you eat **crackers**?

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

100. How often did you eat **corn bread** or **corn muffins**?

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

101. How often did you eat **biscuits**?

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

102. How often did you eat **potato chips** (including low-fat, fat-free, or low-salt)?

☐ NEVER (GO TO QUESTION 103)

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

102a. How often were the potato chips you ate **low-fat** or **fat-free** chips?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

103. How often did you eat **tortilla chips** or **corn chips** (including low-fat, fat-free, or low-salt)?

☐ NEVER (GO TO QUESTION 104)

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

103a. How often were the tortilla or corn chips you ate **low-fat** or **fat-free** chips?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

104. How often did you eat **popcorn** (including low-fat)?

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

105. How often did you eat **pretzels**?

☐ NEVER

- ☐ 1-6 times per year
- ☐ 7-11 times per year
- ☐ 1 time per month
- ☐ 2-3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3-4 times per week
- ☐ 5-6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Over the past 12 months...

106. How often did you eat **peanuts, walnuts, seeds, or other nuts**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

107. How often did you eat **granola bars**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

108. How often did you eat **yogurt** (NOT including frozen yogurt)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

109. How often did you eat **cottage cheese** (including low-fat)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

110. How often did you eat **cheese** (including low-fat; including on cheeseburgers or in sandwiches or subs)?

- ☐ NEVER (GO TO QUESTION 111)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Question 111 appears in the next column.

110a. How often was the cheese you ate **light or low-fat cheese**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

111. How often did you eat **frozen yogurt, sorbet, or ices** (including low-fat or fat-free)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

112. How often did you eat **ice cream, ice cream bars, or sherbet** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 113)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

112a. How often was the ice cream you ate **light, low-fat, or fat-free ice cream or sherbet**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

113. How often did you eat **pudding or custard**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

114. How often did you eat **cake** (including low-fat or fat-free)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Over the past 12 months...

115. How often did you eat **cookies or brownies** (including low-fat or fat-free)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

116. How often did you eat **doughnuts, sweet rolls, Danish, or pop-tarts**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

117. How often did you eat **sweet muffins or dessert breads** (including low-fat or fat-free)?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

118. How often did you eat **fruit crisp, cobbler, or strudel**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

119. How often did you eat **pie**?

- ☐ NEVER (GO TO QUESTION 120)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

Question 120 appears in the next column.

119a. How often was the pie you ate **fruit pie** (such as apple, cherry, peach, blueberry, or others)?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

120. How often did you eat **chocolate candy**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

121. How often did you eat **other candy**?

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

122. How often did you eat **eggs, egg whites, or egg substitutes** (NOT counting eggs in baked goods and desserts)? (Please include eggs in salads, quiche, and souffles.)

- ☐ NEVER (GO TO QUESTION 123)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

122a. How often were the eggs you ate **egg substitutes**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always



Question 123 appears on the next page.

Over the past 12 months...

122b. How often were the eggs you ate **egg whites only**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

122c. How often were the eggs you ate **regular whole eggs**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

122d. How often were the eggs you ate part of **egg salad**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

123. How many cups of **coffee**, caffeinated or decaffeinated, did you drink?

☐ NONE (GO TO QUESTION 124)

- | | |
|---|--|
| <input type="radio"/> Less than 1 cup per month | <input type="radio"/> 5-6 cups per week |
| <input type="radio"/> 1-3 cups per month | <input type="radio"/> 1 cup per day |
| <input type="radio"/> 1 cup per week | <input type="radio"/> 2-3 cups per day |
| <input type="radio"/> 2-4 cups per week | <input type="radio"/> 4-5 cups per day |
| | <input type="radio"/> 6 or more cups per day |

123a. How often was the coffee you drank **decaffeinated**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

124. How many glasses of **ICED tea**, caffeinated or decaffeinated, did you drink?

☐ NONE (GO TO QUESTION 125)

- | | |
|---|--|
| <input type="radio"/> Less than 1 cup per month | <input type="radio"/> 5-6 cups per week |
| <input type="radio"/> 1-3 cups per month | <input type="radio"/> 1 cup per day |
| <input type="radio"/> 1 cup per week | <input type="radio"/> 2-3 cups per day |
| <input type="radio"/> 2-4 cups per week | <input type="radio"/> 4-5 cups per day |
| | <input type="radio"/> 6 or more cups per day |

Question 125 appears in the next column.

124a. How often was the iced tea you drank **decaffeinated or herbal tea**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

125. How many cups of **HOT tea**, caffeinated or decaffeinated, did you drink?

☐ NONE (GO TO QUESTION 126)

- | | |
|---|--|
| <input type="radio"/> Less than 1 cup per month | <input type="radio"/> 5-6 cups per week |
| <input type="radio"/> 1-3 cups per month | <input type="radio"/> 1 cup per day |
| <input type="radio"/> 1 cup per week | <input type="radio"/> 2-3 cups per day |
| <input type="radio"/> 2-4 cups per week | <input type="radio"/> 4-5 cups per day |
| | <input type="radio"/> 6 or more cups per day |

125a. How often was the hot tea you drank **decaffeinated or herbal tea**?

- ☐ Almost never or never
- ☐ About 1/4 of the time
- ☐ About 1/2 of the time
- ☐ About 3/4 of the time
- ☐ Almost always or always

126. How often did you add **sugar or honey** to your coffee or tea?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> Less than 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 1-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 2-4 times per week | <input type="radio"/> 4-5 times per day |
| | <input type="radio"/> 6 or more times per day |

127. How often did you add **artificial sweetener** to your coffee or tea?

☐ NEVER

- | | |
|--|---|
| <input type="radio"/> Less than 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 1-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 2-4 times per week | <input type="radio"/> 4-5 times per day |
| | <input type="radio"/> 6 or more times per day |



Over the past 12 months...

128. How often was **non-dairy creamer** added to your coffee or tea?

- ☐ NEVER (GO TO QUESTION 129)
- | | |
|--|---|
| <input type="radio"/> Less than 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 1-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 2-4 times per week | <input type="radio"/> 4-5 times per day |
| | <input type="radio"/> 6 or more times per day |

128a. What kind of **non-dairy creamer** did you usually use?

- ☐ Regular powdered
☐ Low-fat or fat-free powdered
☐ Regular liquid
☐ Low-fat or fat-free liquid

129. How often was **cream** or **half and half** added to your coffee or tea?

- ☐ NEVER
- | | |
|--|---|
| <input type="radio"/> Less than 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 1-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 2-4 times per week | <input type="radio"/> 4-5 times per day |
| | <input type="radio"/> 6 or more times per day |

130. How often was **milk** added to your coffee or tea?

- ☐ NEVER (GO TO QUESTION 131)
- | | |
|--|---|
| <input type="radio"/> Less than 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 1-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2-3 times per day |
| <input type="radio"/> 2-4 times per week | <input type="radio"/> 4-5 times per day |
| | <input type="radio"/> 6 or more times per day |

130a. What kind of **milk** was usually added to your coffee or tea?

- ☐ Whole milk
☐ 2% milk
☐ 1% milk
☐ Skim, nonfat, or 1/2% milk
☐ Evaporated or condensed (canned) milk
☐ Soy milk
☐ Rice milk
☐ Raw, unpasteurized milk
☐ Other

Question 131 appears in the next column.

131. How often was **sugar** or **honey** added to foods you ate? (Please do not include sugar in coffee, tea, other beverages, or baked goods.)

- ☐ NEVER
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

132. How often did you eat **margarine** on breads, bagels, English muffins, other muffins, pancakes, or waffles?

- ☐ NEVER (GO TO QUESTION 133)
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

132a. How often was the margarine you ate on these breads **low-fat** or **fat-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

133. How often did you eat **butter** on breads, bagels, English muffins, other muffins, pancakes, or waffles?

- ☐ NEVER (GO TO QUESTION 134)
- | | |
|---|---|
| <input type="radio"/> 1-6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7-11 times per year | <input type="radio"/> 3-4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5-6 times per week |
| <input type="radio"/> 2-3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

133a. How often was the butter you ate on these breads **low-fat** or **fat-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

Question 134 appears on the next page.

Over the past 12 months...

134. How often did you eat **margarine** on potatoes, cooked vegetables, rice, grains, or beans?

- ☐ NEVER (GO TO QUESTION 135)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

134a. How often was the margarine you ate on these cooked potatoes, cooked vegetables, rice, grains, or beans **low-fat** or **fat-free**?

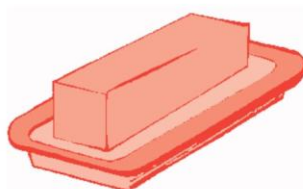
- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

135. How often did you eat **butter** on potatoes, cooked vegetables, rice, grains, or beans?

- ☐ NEVER (GO TO QUESTION 136)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

135a. How often was the butter you ate on these cooked potatoes, cooked vegetables, rice, grains, or beans **low-fat** or **fat-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always



Question 136 appears in the next column.

136. How often did you eat **mayonnaise** as a spread or as part of food mixtures?

- ☐ NEVER (GO TO QUESTION 137)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

136a. How often was the mayonnaise you ate **low-fat** or **fat-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

137. How often did you eat **cream cheese**?

- ☐ NEVER (GO TO QUESTION 138)
- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

137a. How often was the cream cheese you ate **low-fat** or **fat-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always



Question 138 appears on the next page.

Over the past 12 months...

138. How often did you eat **sour cream**?

☐ NEVER (GO TO QUESTION 139)

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

138a. How often was the sour cream you ate **low-fat** or **fat-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

Question 139 appears in the next column.

139. How often did you eat foods with **oils added** or with **oils used in cooking** (do not include baked goods or salads)?

☐ NEVER

- | | |
|---|---|
| <input type="radio"/> 1–6 times per year | <input type="radio"/> 2 times per week |
| <input type="radio"/> 7–11 times per year | <input type="radio"/> 3–4 times per week |
| <input type="radio"/> 1 time per month | <input type="radio"/> 5–6 times per week |
| <input type="radio"/> 2–3 times per month | <input type="radio"/> 1 time per day |
| <input type="radio"/> 1 time per week | <input type="radio"/> 2 or more times per day |

139a. What kind of **oils** do you **usually eat**?
(Mark all that apply.)

- ☐ Olive
☐ Corn
☐ Canola/rapeseed
☐ Other

*Thank you **very much** for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:*

- Did not skip any pages,
- Completely blackened-in each answer, and
- Completely erased any changes you may have made.

If found, please return to:

Janice Hall
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1650 Research Blvd
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